IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

UNIVERSITY OF MASSACHUSETTS and CARMEL LABORATORIES, LLC, Plaintiffs, v. L'ORÉAL USA, INC., Defendant.	C.A. No. 17-868-CFC-SRF

JOINT CLAIM CONSTRUCTION BRIEF

TABLE OF CONTENTS

TABLE OF AUTHORITIES

Page(s)

Cases

Statutes

Rules

Regulations

Pursuant to Paragraph 16 of the Court's Scheduling Order (D.I. 46) (as amended), Plaintiffs University of Massachusetts and Carmel Laboratories, LLC (together "Plaintiffs") and Defendant L'Oréal USA, Inc. ("Defendant") (collectively, the "Parties") provide this Joint Claim Construction Brief.

There is only one term in dispute, which is, "wherein the adenosine concentration applied to the dermal cells is . . . ." *See* U.S. Patent No. 6,423,327 ("'327 Patent"), claim 1; Patent No. 6,645,513 ("'513 Patent"), claim 1 (D.I. 77 Ex. 1 and 2, respectively).

The Parties' positions with respect to this term are below.

Plaintiffs' Construction	Defendant's Construction
Plain and ordinary meaning. Alternatively, if construed, "wherein the adenosine concentration that reaches the dermal cell layer is"	"wherein the adenosine concentration applied to the skin containing the dermal cells is"

I. PLAINTIFFS' OPENING POSITION

Plaintiffs assert that Defendant infringes claims of the '327 and '513 Patents. Both patents disclose methods to enhance the condition of skin without increasing dermal cell proliferation, by applying recited ranges of adenosine "to the dermal cells." '327 Patent at claim 1; '513 Patent at claim 1.

Defendant proposes a strained construction that is inconsistent with the intrinsic evidence, relies on a misreading of the patent prosecution history, and ignores the plain meaning of ordinary words the asserted patents use unambiguously.

At its core, Defendant wishes to interpret the claims in a manner inconsistent with basic science—that the "epidermis" is the same as the "dermis." But even children know the difference between these structures. *See, e.g.*, American Academy of Dermatology, *What Kids Should Know About the Layers of Skin*, *available at* https://www.aad.org/teach-healthy-habits/skin-layers ("Epidermis is the top layer of the skin, the part of the skin you see. Dermis is the second layer of skin. It's much thicker and does a lot for your body."); *see also Phillips v. AWH Corp.*, 415 F.3d 1303, 1314 (Fed. Cir. 2005) ("In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words."). And nothing in the prosecution history comes close to a "clear and unmistakable disclaimer" that would overcome this fundamental science. *Ecolab, Inc., v. FMC Corp.*, 569 F.3d 1335, 1342 (Fed. Cir. 2009).

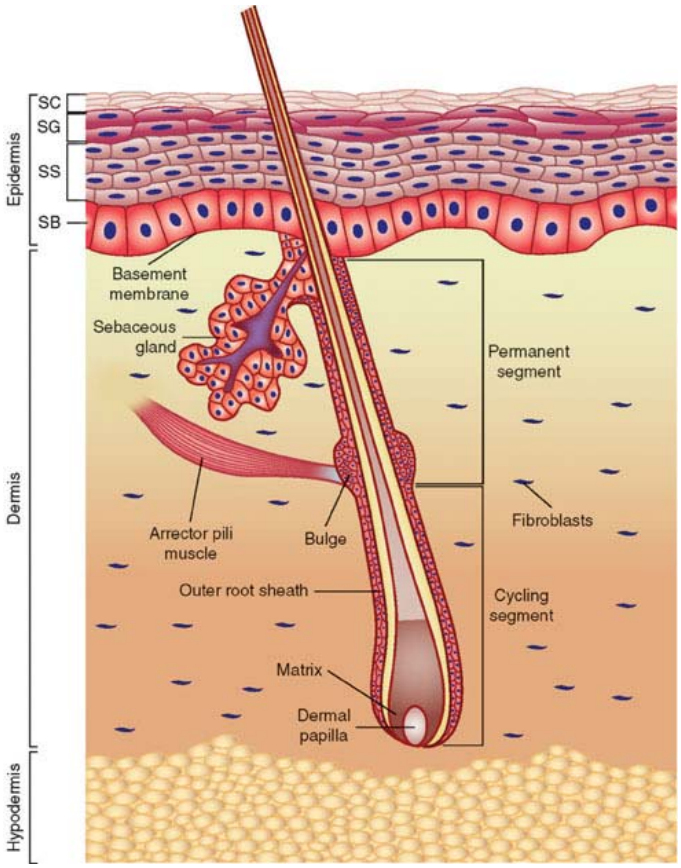
Plaintiffs, by contrast, propose either no construction or, if the Court is inclined to clarify this term, one based on its plain and ordinary meaning. *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) ("[W]e indulge a 'heavy presumption' that a claim term carries its ordinary and customary meaning.") (quoting *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed. Cir. 1999)).

The Parties have already briefed the same claim construction issue for the same term, in conjunction with Defendant's petitions for *inter partes* review of both asserted patents. The Patent and Trademark Office ("PTO") agreed with Plaintiffs that this term needs no construction, and on that basis, denied Defendant's petitions. As explained further below, this Court should do the same.

A. Overview of the Patented Inventions

The asserted patents teach that "[s]kin includes a surface layer, known as the epidermis, and a deeper connective tissue layer, known as the dermis." '327 Patent[1] at 1:19-20. "The dermis is composed of a variety of cells types, including fibroblasts." *Id.* at 1:23-24. In other words, "the skin" is comprised of both the epidermis and the dermis; "dermal cells" are cells in the dermal layer of the skin, and may include dermal fibroblasts. "As skin ages, or is exposed to UV light and other environmental insults," the "dermis becomes thinner and the number of skin fibroblasts declines." *Id.* at 1:25-33. In turn, "products of the fibroblasts," such as the proteins "collagen and proteoglycans," decrease in "abundance and function," and play a "major role in wrinkled and damaged skin." *Id.*

[1] The asserted patents share a nearly identical specification, and Plaintiffs reference only the '327 Patent specification for convenience.



David J. Wong and Howard Y. Chang, *Skin Tissue Engineering* (Harvard Stem Cell Institute 2008), *available at* https://www.ncbi.nlm.nih.gov/books/NBK27029/.

Plaintiffs use this publicly-available diagram as an illustrative example, but countless other sources reiterate this basic scientific fact. *See, e.g.*, Ex. 5 (Decision Denying *Inter Partes* Review of the '327 Patent) ("'327 IPR Denial") at 8 (App'x A0179) ("There is no dispute that the skin is comprised of multiple layers.") (depicting a figure illustrating "[t]he multiple layers of skin").

The inventors of the asserted patents—Doctors James G. Dobson, Jr. and Michael Ethier, both formerly of the University of Massachusetts—sought to address aging and damaged skin using their discoveries regarding adenosine.

Adenosine is a naturally occurring purine nucleoside that plays an important role in a variety of biochemical processes. Prior inventions had disclosed using adenosine to treat human skin, but prior art taught using adenosine to increase dermal cell proliferation—i.e., treating the thinning dermis by increasing the number of dermal cells. But dermal cell proliferation can be detrimental and "cause scarring, discoloration, and a variety of other skin anomalies associated with hyperplasia." Ex. 2 (excerpts of the file history of the '327 Patent) ("'327 File History") at 84 (App'x A0078).

Doctors Dobson and Ethier discovered that the benefits of adenosine could be harnessed without increasing dermal cell proliferation. Specifically, they discovered that low concentrations of adenosine applied to the dermal cells could be used to "enhance[e] the condition of skin" by "stimulat[ing] DNA synthesis, increas[ing] protein synthesis, and increas[ing] cell size" in "human skin fibroblasts," but without "caus[ing] proliferation of the dermal cells." '327 Patent at 1:37-41; 1:59-60; 1:66-67. That is, in direct contrast to prior art, the claimed inventions teach that the best way to treat the thinning dermis with adenosine is not to increase the number of dermal cells, but to use a low concentration of adenosine to enhance the size and function of existing dermal cells.

The patents disclose that their methods can be used, for example, to "enhance[e] the condition of aged skin," on "subjects having otherwise damaged

skin, e.g., wrinkled skin and skin with a non-proliferative disorder," and "prophylactically on a subject to minimize deterioration of skin condition associated with aging or environmental factors, such as photodamage." *Id.* at 3:23-35. Both patents teach that adenosine may be "applied to the dermal cells" for these uses "preferably applied by topical routes," where such "topical application" results in "the penetration of the adenosine into skin tissue." *Id.* at 5:10-14. But in order to achieve the disclosed benefits of "stimulate[d] DNA synthesis, increase[d] protein synthesis, and increases in cell size" to "fibroblasts," adenosine must by necessity penetrate to the dermal layer of skin. *Id.* at 1:37-41; *see also id.* at 9:5-51 (disclosing, for example, "increased cell size" from direct application to dermal fibroblasts of adenosine in the amount of 10^{-4} M). Simply put, while "the skin" includes both the epidermis and the dermis, *id.* at 1:19-24, the patents teach that the recited concentration of adenosine must penetrate "to the dermal cells" to obtain the claimed skin enhancement.

The '327 Patent issued first. Claim 1 of the '327 Patent, the only independent claim, recites a method comprising "topically applying to the skin a composition comprising a concentration of adenosine in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, wherein the adenosine concentration applied to the dermal cells is 10^{-4} M to 10^{-7} M." The '327 Patent also discloses a number of dependent claims. The '513 Patent issued second,

and built on the inventorship of the '327 Patent. Claim 1 of the '513 Patent, the only independent claim, recites a method comprising "topically applying to the skin a composition comprising a concentration of adenosine in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, wherein the adenosine concentration applied to the dermal cells is 10^{-3} M to 10^{-7} M." The '513 Patent also discloses a number of dependent claims.

B. Defendant's Construction Was Rejected by the PTO

Defendant previously petitioned the PTO for *inter partes* review of both asserted patents. In its petitions, Defendant requested claim construction of the same term at issue now, and there, contended the term should be construed as reciting "a concentration of adenosine ***in the composition*** that is topically applied to an unbroken, epidermal layer of a region of skin containing the dermal cells." '327 IPR Denial at 8 (App'x A0179) (emphasis in original). Although Defendant has shortened its proffered construction of this term somewhat since its failed petitions, the construction's import remains the same. Both in its petitions and now, "[t]he fundamental question presented by [Defendant] in connection with its proposed construction is whether the recited concentration [of adenosine] is applied to the dermal cells or the epidermal cells." *Id.* at 9 (App'x A0180). To the extent Defendant now argues it does not intend to point to the epidermis with its construction, which calls for the recited concentrations of adenosine to be applied to "the skin containing

the dermal cells," its construction merely creates ambiguity and confusion where there is none in the asserted claims. "[T]he skin" is comprised of both the epidermis and the dermis; only the dermis "contain[s] the dermal cells," but the claims already plainly state that the recited concentration of adenosine is to be applied "to the dermal cells."

Plaintiffs argued to the PTO, and still maintain, that the term should be construed according to its plain and ordinary meaning, and that "the recited concentration is the concentration that is applied to the dermal cells." *See id.* at 8 (App'x A0179) (emphasis in original); *see also* Ex. 6 (Decision Denying Inter Partes Review of the '513 Patent) ("'513 IPR Denial") at 10 (App'x A0202) (same constructions).

Defendant's strained construction that the claims really mean "applied to the skin" (i.e., the epidermis) was squarely—and correctly—rejected by the PTO in its decisions denying *inter partes* review of both asserted patents. The three-judge IPR panel reviewed Defendant's construction in "a district court-type claim construction like that provided in *Phillips*," and found that "the disputed claim language is unambiguous [and] requires an adenosine concentration 'applied to the dermal cells.'" '327 IPR Denial at 6, 15 (App'x A0177, A0186); '513 IPR Denial at 6, 14 (App'x A0198, A0206). Accordingly, the PTO construed "the 'concentration applied to the dermal cells' to mean what it says—that the recited concentration is

the concentration that is applied to the dermal cells." '327 IPR Denial at 15 (App'x A0186); '513 IPR Denial at 14 (App'x A0206). On that basis, the PTO denied Defendant's petition for *inter partes* review because the prior art cited by Defendant had no "evidence reflecting the concentration of adenosine applied to the dermal cells," and therefore Defendant did not have a reasonable likelihood of prevailing in its invalidity arguments. '327 IPR Denial at 16-19 (App'x A0187-90); '513 IPR Denial at 15-18 (App'x A0207-10).

Defendant sought reconsideration of that decision, but the PTO confirmed the claims mean exactly what they say:

> Our construction gives the term "dermal cells" its ordinary meaning by construing it to refer to "dermal cells"—i.e., the dermis or dermal layer. We do not find in the record, and Petitioner does not suggest, another way to interpret the limitation "concentration applied to the dermal cells" consistent with the ordinary meaning of the words "dermal cells." . . . [T]here is no meaningful difference between the "epidermal layer of a region of the skin containing the dermal cells" recited in Petitioner's proposed claim construction, and the epidermis. Petitioner's proposed construction is, thus, contrary to the language of the claim, because it changes the meaning of "dermal cells" to "epidermal cells." . . . [T]he Specification discloses not only that adenosine may be topically applied to the epidermal layer of the skin, but also that adenosine so applied will penetrate the epidermis to reach the dermal layer. . . Topical application of adenosine will, therefore, result in adenosine being brought in contact with both the epidermis and the dermis. . . . [T]he Specification provides examples in which a concentration of adenosine matching the high end recited in the claims (10^{-4} M) is applied directly to dermal cells (fibroblasts), suggesting that the inventors considered it desirable for the dermal cells to receive the claimed concentration of adenosine. <u>In this context, the meaning of claim 1 is clear: adenosine is first topically applied to the epidermal layer of the skin and, only after it penetrates this outer skin layer, is a</u>

> specific concentration (10^{-4} M to 10^{-7} M) of the adenosine "applied" to the dermal cells.

Ex. 7 (Decision Denying Reconsideration for the '327 Patent) ("'327 Reconsideration Denial") at 5-6 (App'x A0217-18) (emphasis added); *see also* Ex. 8 (Decision Denying Reconsideration for the '513 Patent) ("'513 Reconsideration Denial") at 5-6 (App'x A0229-30) (same).

Defendant now reprises the same twice-debunked claim construction argument, hoping this Court will rewrite these unambiguous claims where the PTO was unwilling to do so. The Court should instead affirm that the claims mean what they say.

C. Defendant Attempts to Rewrite the Claims and Defies the Intrinsic Evidence with its Proffered Construction

Both claims at issue recite that the claimed concentration of adenosine is "applied to the dermal cells." '327 Patent at claim 1, '513 Patent at claim 1. Defendant would rewrite the claims such that the adenosine is "applied to the skin containing the dermal cells"—i.e., applied to the epidermis.

Claim interpretation starts with the claim language itself. *Phillips*, 415 F.3d at 1312. In addition to the language of the claims, it is "entirely appropriate" for a court "to rely heavily on the [specification] for guidance as to the meaning of the claims." *Id*. at 1317. Prosecution history may be helpful, but because it "represents an ongoing negotiation between the PTO and the applicant, rather than the final product

of that negotiation, it often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Id.* (citations omitted). Courts may consider extrinsic evidence as well, but "it is less significant than the intrinsic record in determining the legally operative meaning of claim language." *Id.* (citations and quotations omitted).

As already explained multiple times by the PTO, Defendant's construction contradicts the claim language, the specification, and the prosecution history, and should be rejected in favor of the term's plain and ordinary meaning.

The Claim Language

The claim language distinguishes between "the skin" and the "dermal cells." Claim 1 of the '327 Patent recites:

> A method for enhancing the condition of unbroken skin of a mammal by reducing one or more of wrinkling, roughness, dryness, or laxity of the skin, without increasing dermal cell proliferation, the method comprising topically applying to the skin a composition comprising a concentration of adenosine in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, wherein the adenosine concentration applied to the dermal cells is 10^{-4} M to 10^{-7} M.

Claim 1 (emphasis added); *see also* claim 1 of the '513 Patent (same, but the "adenosine concentration applied to the dermal cells is 10^{-3} M to 10^{-7} M"). Thus, the claim discloses a method whereby a composition containing adenosine is "topically appl[ied] to the skin" and "the adenosine concentration applied to the dermal cells is 10^{-4} M to 10^{-7} M" (or, in the case of the '513 Patent, 10^{-3} M to 10^{-7} M).

The plain and ordinary meaning of "dermal cells" is dermal cells—i.e., cells in the dermal layer of skin. No "elaborate interpretation" is needed for terms whose ordinary meanings are apparent. *Phillips*, 415 F.3d at 1314 (citations and quotations omitted). Defendant's construction would change "the dermal cells" to "the skin containing the dermal cells," a bald attempt to avoid liability by turning the claim language on its head. The claim plainly distinguishes between "the skin" and "the dermal cells" (a specific area of the skin), where a composition is "topically applied to the skin," and the recited adenosine concentration is "applied to the dermal cells." If the inventors had wanted the adenosine to be applied "to the skin," rather than "to the dermal cells," they would have said so. *See Bd. Of Regents of the Univ. of Tex. Sys. v. BENQ Am. Corp.*, 533 F.3d 1362, 1371 (Fed. Cir. 2008) ("Different claim terms are presumed to have different meanings."); *Merck & Co., Inc. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1372 (Fed. Cir. 2005) ("A claim construction that gives meaning to all the terms of the claim is preferred over one that does not do so."); '327 IPR Denial at 9-10 (App'x A0180-81) ("One would expect that if the Patent Owner had intended both 'applications' recited in the claim 1 to be made to the same cells, Patent Owner would have used the same term to describe both applications."). Defendant's construction defies the words of the claim it proposes to construe, and should be rejected.

The Specification

The specification further supports Plaintiffs' plain and ordinary meaning interpretation of this term. The specification is "[u]sually dispositive; it is the single best guide to the meaning of a disputed term." *Phillips*, 415 F.3d at 1315 (citations omitted). The very first sentence of the specification confirms the straightforward fact that the skin is composed of multiple layers: "Skin includes a surface layer, known as the epidermis, and a deeper connective tissue layer, known as the dermis." '327 Patent at 1:20-21. The specification explains that compositions containing adenosine are "preferably applied by topical routes to exert local therapeutic results," but, as explained above, in order to achieve the disclosed benefits of "stimulate[d] DNA synthesis, increase[d] protein synthesis, and increases in cell size" to "fibroblasts," adenosine must reach the dermal layer. *Id.* at 1:37-41; 5:10-13; *see also id.* at 1:24-25 ("The dermis is composed of a variety of cell types, including fibroblasts"); '327 Reconsideration Denial at 6-7 (App'x A0218-19) (the "ordinary meaning of 'apply'" is "to bring into physical contact with or close proximity to") (citations omitted). Indeed, the specification describes experiments in which adenosine within the claimed range (10^{-4} M) was applied directly to dermal fibroblasts in order to demonstrate the effect of that concentration of adenosine on dermal cells. *See* '327 Patent at 9:5-51 (disclosing "increased cell size"). This

confirms the inventors intended the claimed ranges of adenosine to be applied to the dermal cells.

Moreover, the specification expressly discloses that adenosine may penetrate from the epidermis to the dermis: "For topical application, the penetration of the adenosine into skin tissue may be enhanced by a variety of methods known to those of ordinary skill in the art." *Id.* at 5:10-16 (emphasis added); *see also id.* at 5:19-25 ("Preferably, the penetration resulting from these methods is enhanced with a chemical transdermal delivery agent such as dimethyl sulfoxide (DMSO) or the nonionic surfactant, n-decylmethyl sulfoxide (NDMS), as described in Choi et al., Pharmaceutical Res., 7(11): 1099, 1990.") (emphasis added); claim 9 ("The method of claim 1, wherein the composition further comprises a transdermal delivery agent.").

Accordingly, Defendant's construction flouts the specification, which does not equate "the skin" and "the dermal cells," but instead relies on the distinction between those terms. "In this context, the meaning of claim 1 is clear: adenosine is first topically applied to the epidermal layer of the skin and, only after it penetrates this outer skin layer, is a specific concentration (10^{-4} M to 10^{-7} M) of the adenosine 'applied' to the dermal cells." '327 Reconsideration Denial at 6 (App'x A0218).

Prosecution History

In the face of unambiguous evidence that the claims mean what they say, Defendant relied heavily on prosecution history in its petition for *inter partes* review, arguing the inventors disavowed the plain and ordinary meaning of "applied to the dermal cells" during prosecution. Prosecution history "often lacks the clarity of the specification and thus is less useful for claim construction purposes." *Phillips*, 415 F.3d at 1317. Accordingly, the Federal Circuit requires "a clear and unmistakable disavowal of scope during prosecution." *Purdue Pharma L.P. v. Endo Pharm. Inc.*, 438 F.3d 1123, 1136 (Fed. Cir. 2006). Here, the prosecution history confirms that "applied to the dermal cells" means "applied to the dermal cells."

The claims of the '327 Patent were allowed on March 18, 2002. In the Notice of Allowability, the Examiner characterized the claims as being directed to a "method of enhancing the condition of unbroken skin by reducing wrinkling or dryness or laxity of skin, without increasing dermal cell proliferation, where the method comprises administering adenosine at a concentration of 10^{-4} M to 10^{-7} M, to the skin." '327 File History at 117 (App'x A0101) (emphasis added). The inventors responded with comments on May 17, 2002, clarifying that the recited concentration of adenosine is not administered "to the skin," but instead, "the claimed concentration of adenosine is applied to the dermal cells." *Id.* at 123 (App'x A0103). As the IPR panel stated, "Patent Owner expressly corrected the Examiner .

. . . This suggests that the Patent Owner did not intend for the concentration recited in the claims to be the concentration applied to the skin." '327 Reconsideration Denial at 9-10 (App'x A0221-22).

In its petitions for *inter partes* review, Defendant nonetheless argued that the inventors disclaimed the plain and ordinary meaning of "applied to the dermal cells" during prosecution. The '327 Patent was initially disallowed as allegedly anticipated by certain prior art references. The inventors argued those references could be distinguished because, where the prior art taught "the use of adenosine for increasing cell proliferation in human skin . . . applicants' claims require no increase in dermal cell proliferation, because such excess cell proliferation can cause scarring, discoloration, and a variety of other skin anomalies associated with hyperplasia." '327 File History at 84 (App'x A0078). According to the inventors, any argument that the prior art references disclosed adenosine in the range of "10^{-4} M and 10^{-5} M concentrations [as] recited in the claims of the present invention" was not "supported by reality," because "the presently claimed invention is based on the demonstration that the recited concentrations of adenosine do not increase cell proliferation . . . [which] is the exact opposite of the assertions in the German patent application . . . [and thus] the German patent application does not disclose the same invention as the proposed claims in the present application." *Id*. With their response, the inventors submitted testing results in which adenosine at concentrations of 10^{-4} M and 10^{-5} M

was applied directly to dermal cells (not generically to "the skin"), which resulted in no dermal cell proliferation. *Id*. at 82-83, 107-09 (App'x A0076-77, A0095-97). As explained by the PTO, where the inventors "submitted results from tests in which adenosine was applied directly to dermal cells (fibroblasts) at concentrations of 10^{-4} M and 10^{-5} M. . . . [t]his suggests that the inventors contemplated dermal cells receiving the recited concentration of adenosine." '327 Reconsideration Denial at 9 (App'x A0221) (citing the '327 File History).

Defendant distorted these statements in support of its petition for *inter partes* review, arguing the inventors "compared prior art concentrations of adenosine that were recited as a percentage of the <u>total weight of the composition to the concentration recited in the claims as being 'applied to the dermal cells</u>.'" '327 Reconsideration Denial at 7 (App'x A0219) (emphasis in original). Thus, according to Defendant, the inventors disclaimed the plain and ordinary meaning of "applied to the dermal cells," in favor of Defendant's strained construction that "applied to the dermal cells" means "applied to the skin"—i.e., the claimed ranges of adenosine recite the amount applied topically (as a "percentage of the total weight of the composition"), rather than the amount that penetrates to the dermal cells.

Where, as here, an accused infringer relies upon prosecution history in an effort to change the meaning of the claims, the accused infringer must point to "a clear and unmistakable disavowal of scope during prosecution." *Purdue Pharma*

L.P. v. Endo Pharm. Inc., 438 F.3d 1123, 1136 (Fed. Cir. 2006). The Federal Circuit requires "unambiguous disavowals" of the plain and ordinary meaning because, "while the prosecution history can inform whether the inventor limited the claim scope in the course of prosecution, it often produces ambiguities created by ongoing negotiations between the inventor and the PTO." *Grober v. Mako Prods., Inc.*, 686 F.3d 1335, 1341 (Fed. Cir. 2012) (citing *Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1289 (Fed. Cir. 2009)). This standard is "exacting." *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1366 (Fed. Cir. 2012).

There was no "clear and unmistakable disavowal" here. On the contrary, the inventors distinguished the prior art references on the grounds that they disclosed an increase in dermal cell proliferation, the "exact opposite" of the invention disclosed in the '327 Patent. '327 File History at 84 (App'x A0078). Indeed, to further underscore that "applied to the dermal cells" means "applied to the dermal cells," the inventors submitted testing results to the Examiner, in which they applied adenosine in the relevant range (10^{-4} M and 10^{-5} M) directly to dermal cells—not generally to the skin or to the epidermis.

Although Defendant will likely point to the same isolated statements in which the inventors compared the concentration of adenosine in a prior art reference to the concentration of adenosine in the claimed invention, the inventors did so only to show the "extremely broad range of adenosine concentrations listed in . . . [the

German patent application] is not supported by reality." '327 Reconsideration Denial at 8 (App'x A0220) (citing the '327 File History). "Even if an isolated statement appears to disclaim subject matter, the prosecution history as a whole may demonstrate that the patentee committed no clear and unmistakable disclaimer." *Ecolab, Inc., v. FMC Corp.*, 569 F.3d 1335, 1342 (Fed. Cir. 2009). Where the inventors submitted testing results showing direct application of adenosine in the claimed range to the dermal cells, and (after comparing the prior art references to the claimed invention) corrected the Examiner when the Examiner characterized the invention as requiring the claimed range of adenosine to be applied "to the skin," the prosecution history as a whole supports that the claims mean precisely what they say.

The PTO agreed with Plaintiffs' interpretation of the prosecution history, and denied Defendant's petition for *inter partes* review:

> Patent Owner did not use this statement to distinguish the claimed adenosine concentration from a concentration disclosed in the prior art. . . . Patent Owner argued that, although [the German patent application] disclosed a concentration of adenosine within the recited range, in contrast to the challenged claims, [it] taught (incorrectly accordingly to the Patent Owner) that this level of adenosine increases cell proliferation. . . . Patent Owner's comparison of the claimed concentration to a prior art concentration . . . does not "clearly redefine" the phrase "applied to the dermal cells" or alter the scope of the claims such that the recited concentration of adenosine need not reach the dermal cells. Nor does it disclaim subject matter found in the prior art or, otherwise, "unmistakably" disavow application of the recited concentration to the dermal cells.

'327 Reconsideration Denial at 8-9 (App'x A0220-21); *see also id.* at 9-10 (App'x A0221-22) ("Patent Owner expressly corrected the Examiner . . . This suggests that the Patent Owner did not intend for the concentration recited in the claims to be the concentration applied to the skin.").[2]

As already decided repeatedly by the PTO, the claims, specification, and prosecution history alike confirm that "applied to the dermal cells" means exactly what it says. The Court should affirm that "dermal cells" means "dermal cells," and order that this term has its plain and ordinary meaning.

II. DEFENDANT'S ANSWERING POSITION[3]

A. Introduction

Claim construction involves careful consideration of the claim language, as understood in light of the intrinsic record as a whole. Plaintiffs encourage the Court

[2] Defendant sought to submit a reply to the PTO in further support of its petitions, in order to lodge further argument related to statements made during prosecution of U.S. Patent Application No. 10/680,370 ("the '370 application"), which claims priority to the '327 and '513 Patents. The PTO denied this request as untimely, but more importantly irrelevant because "the arguments made by Patent Owner in connection with the '370 application are substantially similar to those it made – and disclosed to the Board – in connection with prosecution of the application discussed herein. As such, we consider the arguments based the '370 application to be cumulative to arguments already of record." '327 IPR Denial at 11-12 n.5 (App'x A0182-83) (citations omitted). To the extent Defendant reprises this cumulative argument here, it likewise does not evince a clear and unmistakable disclaimer.

[3] By providing the proposed construction herein, L'Oréal USA does not waive any invalidity defenses, including under 35 U.S.C. § 112, as set forth in its Initial Invalidity Contentions.

to shirk this analysis, and instead simply follow the approach taken by the Patent Trial and Appeals Board ("Board") in IPR proceedings addressing the patents-in-suit. The Board's decision, however, misinterpreted key portions of the intrinsic record while overlooking others, and is contrary to fundamental tenets of claim construction law. (*See* Sections II.B, II.C.3.a-b, *infra*.)

The Board was also completely unaware that, as confirmed by Plaintiffs' infringement contentions in this lawsuit, Plaintiffs' claim construction position is no more than a ploy intended to capture ***the very same prior art adenosine concentrations they distinguished to obtain their patents***. Consistent with the claims themselves and the shared specification, Applicants repeatedly told the U.S. Patent and Trademark Office ("PTO") that the claimed concentration ranges referred to the adenosine concentration in the composition topically applied to the skin. In doing so, Applicants distinguished prior art disclosing the use of compositions containing "0.1%" adenosine (which they equated to "3.8 x 10^{-3} M" in the terminology of the patents-in-suit) in light of the "proposed amended claims . . . recit[ing] a maximum concentration of adenosine of 10^{-4} M." ('327 prosecution history at 84-85 (Appx A0078-79).)

Yet, Plaintiffs now contend that L'Oréal USA's products containing the ***identical concentrations of adenosine that Applicants distinguished during prosecution*** (*e.g.*, 0.1% adenosine) somehow infringe the patents-in-suit. To do this,

Plaintiffs seek to contort the claim language of the claims to refer not to the adenosine concentration in the composition, but rather the concentration after it travels through the various layers of the skin and "reaches the dermal cell layer." In other words, Plaintiffs are contending that the patents-in-suit claim two separate adenosine concentrations—one in the composition ("a ***composition*** comprising ***a concentration of adenosine*** in an amount effective to enhance the condition of the skin") and another that "reaches the dermal cell layer" (through the "wherein" clause).[4] As explained below, Plaintiffs' attempted reinterpretation lacks support in the intrinsic record and should be rejected in favor of L'Oréal USA's ordinary-meaning construction.

B. Background

Plaintiffs have accused more than 150 L'Oréal USA products, many of which have been marketed for years, of infringing patents that issued more than 15 years ago and are now expired. These patents are generally directed to methods of enhancing skin condition by topically applying (*i.e.*, to the skin) compositions containing adenosine at certain concentrations ("10^{-4} M to 10^{-7} M" or "10^{-3} M to 10^{-7} M").[5] The parties do not dispute that none of the accused products contain

[4] Unless otherwise noted, all internal quotations and citations have been omitted and all emphases have been added in L'Oréal USA's portions of this brief.

[5] A brief scientific tutorial is provided in the Declaration of Professor Gerald B. Kasting, Ph.D. ("Kasting Decl.," Appx A0240-60), which also addresses how a person of ordinary skill in the art would understand the claim language in the context

adenosine in those concentration ranges. Instead, they contain, for example, 0.1% (*i.e.*, 3.8 x 10^{-3} M, according to the patentees) adenosine, which exceeds the upper bound of any claimed range (either 10^{-3} M or 10^{-4} M). (Kasting Decl., ¶ 27 n.2 (Appx A0256).)

At the time the original application for these patents was filed,[6] it was well-established that adenosine could be topically applied to improve skin condition by, for example, reducing wrinkling and increasing skin firmness. (*E.g.*, '327 prosecution history at 74 (Appx A0070).) For example, two prior art references discussed extensively during prosecution of the patents-in-suit disclosed, *inter alia*, 0.1% adenosine compositions for treating skin. (*See, e.g.*, Hartzshtark at 379 (Appx A0292) (using 0.1% and 0.033% adenosine compositions); German Patent Application DE 195 45 107 A1, at 9-12 (Appx A0091-94) ("DE107") (disclosing the use of, *inter alia*, 0.1% adenosine compositions).)[7] In an attempt to avoid these

---

of the relevant scientific field and the intrinsic record. *See Phillips v. AWH Corp.*, 415 F.3d 1303, 1318 (Fed. Cir. 2005) (en banc) ("[E]xtrinsic evidence in the form of expert testimony can be useful to a court for a variety of purposes, such as to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of the technical aspects of the patent is consistent with that of a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field.").

[6] Both patents-in-suit claim priority to the same application.

[7] Plaintiffs acknowledge, as they must, that "[p]rior inventions had disclosed using adenosine to treat human skin," but then assert that the "prior art taught using adenosine to increase dermal cell proliferation." (*Supra* at 5.) While an attempted distraction, the latter statement is incorrect. For example, DE107 refers only to "cell

prior-art compositions, Plaintiffs asserted that, among other things, the adenosine concentrations were not covered by the claims of the patents-in-suit. (*See* Section II.C.3.a, *infra*.) Today, however, Plaintiffs accuse products that use adenosine at the very concentrations described in Hartzshtark and DE107, such as 0.1%, of infringing those same claims based on their proposed construction of the disputed language. The Board did not have this fact in the IPR proceedings, which are relied upon throughout Plaintiffs' brief.[8]

Moreover, as explained further below, the Board erred by, for example, overlooking black-letter Federal Circuit law regarding the use of "a" and "the" in describing claim elements, which dictate interpreting the claims to refer to a single adenosine concentration, *i.e.*, the concentration in the claimed composition. Likewise, the Board ignored the specification's clear description of "the invention" as applying "therapeutically effective amount[s]" of adenosine in concentrations of "preferably 10^{-3} M to 10^{-7} M, more preferably about 10^{-3} M to 10^{-6} M, and most

---

proliferation" generally, not dermal cell proliferation, and Hartzshtark does not discuss cell proliferation at all. (*E.g.*, DE107 at 2 (Appx A0084); Kasting Decl., ¶¶ 19-20 (Appx A0252-53).)

[8] Such knowledge would have exposed Plaintiffs' construction as an attempt to capture compositions containing the same prior-art adenosine concentrations distinguished during prosecution. *See, e.g., Wilson Sporting Goods Co. v. Hillerich & Bradsby*, 442 F.3d 1322, 1326-27 (Fed. Cir. 2006) (noting the importance of claim construction "tak[ing] place in the context of a specific accused infringing device, [which] provides meaningful context").

preferably about 10^{-4} M . . . to the skin." ('327 patent, 1:39-2:8, 2:13-17, 2:30-34, 2:38-40.)[9]

The Board further erred by viewing the prosecution history solely through the lens of prosecution disclaimer. ('327 IPR Decision at 11-13 (Appx A0182-84); '513 IPR Decision at 10-12 (Appx A0202-04); '327 IPR Rehearing Decision at 7-10 (Appx A0219-22); '513 IPR Rehearing Decision at 7-10 (Appx A0231-34).) Compounding this error, the Board misapprehended the content and significance of Applicants' response to the PTO's Reasons for Allowance during prosecution of the '327 patent, which did not "correct" the Reasons for Allowance. (*See* Section II.C.3.a, *infra*.) In any event, during the '513 patent prosecution, the PTO once again made clear the basis for allowance: "[The i]nstant claims are directed to a method of . . . administering adenosine at a concentration of 10^{-3} M to 10^{-7} M, ***to the skin***." ('513 prosecution history at 74, 83 (Appx A0143, A0145).) Applicants expressed nothing but agreement with this statement, and did not even include the alleged "correction" language (*see* Section II.C.3.b, *infra*), yet the Board did not address this at all in its decisions. (Leaving aside Plaintiffs' disparaging remarks, the Examiner no doubt understood the difference between the dermis and the epidermis, and that

[9] As explained in Section II.C.2 below, the specification also describes "culturing [isolated] fibroblasts in the presence of adenosine," but not in terms of topically applying the above-mentioned "therapeutically effective" concentration ranges.

the context for the claimed concentrations is application to the skin.[10]) Tellingly, Plaintiffs have entirely omitted this fact from their opening brief.[11]

In short, any independent review of the intrinsic record will avoid the numerous errors committed by the Board. *See, e.g.*, *Depuy Orthopaedics, Inc. v. Orthopaedic Hosp.*, No. 12-299, 2016 WL 96164, at *5 (N.D. Ind. Jan. 8, 2016) ("[T]he court owes no deference to the PTAB's claim construction done as part of an inter partes review.").

C. The Intrinsic Evidence Compels Construing the Disputed Claim Term to Refer to the Concentration of Adenosine Applied to the Skin

The phrase "applied to the dermal cells" in the disputed "wherein the adenosine concentration applied to the dermal cells is" claim language should be construed as "applied to the skin containing the dermal cells." This construction follows directly from the claims themselves, the specification, and the prosecution

[10] While the Board focused extensively on the difference between the epidermis and dermis, that is not the focus of the present dispute, which centers on the meaning of the word "applied" in the context of the intrinsic record. In any event, and notwithstanding Plaintiffs' assertions about children, those in the cosmetic industry as well as nurses and doctors understand that "***dermal*** administration" commonly refers to administration to the skin. (Kasting Decl., ¶ 14 (Appx A0246-47).)

[11] Many of the Board's claim construction-related statements relied on by Plaintiffs were made in rejecting petitions for rehearing, which are subject to an exacting abuse-of-discretion standard and rarely successful. *See* 37 C.F.R. § 42.71(c); https://www.foley.com/en/insights/publications/2019/10/ptab-requests-rehearing-face-long-odds.

history. By contrast, Plaintiffs' proposed "plain meaning" construction is contrary to the intrinsic record and basic claim construction principles, and should therefore be rejected.[12]

1. The Claims of the Patents-in-Suit Support L'Oréal USA's Proposed Construction

The language of the claims as a whole identifies a single adenosine concentration, namely the concentration applied to the skin:

> 1. A method for enhancing the condition of unbroken skin of a mammal by reducing one or more of wrinkling, roughness, dryness, or laxity of the skin, without increasing dermal cell proliferation, the method comprising topically applying to the skin a composition comprising ***a concentration of adenosine*** ***in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, wherein the adenosine concentration applied to the dermal cells is 10^{-4} M to 10^{-7} M.***

('327 patent, claim 1.)[13] Claim 1 above is directed to a method of enhancing the skin by topically applying a composition containing adenosine in a given concentration. The adenosine concentration is first introduced and described by reference to the concentration in the ***composition*** that is topically applied—"comprising topically

[12] A construction of "plain meaning" is generally inappropriate where, as here, "the parties present a fundamental dispute regarding the scope of a claim term," *see Eon Corp. IP Holdings v. Silver Spring Networks*, 815 F.3d 1314, 1318 (Fed. Cir. 2016), and Plaintiffs concede as much by offering a proposed interpretation of the alleged "plain meaning."

[13] Claim 1 of the '513 patent is identical, except the concentration range is "10^{-3} M to 10^{-7} M."

applying to the skin ***a composition*** comprising ***a concentration of adenosine in an amount effective***." This reference to the concentration requires that it be present in an "effective" amount to "enhance the condition of the skin," which may require different "amount[s]" depending on where the product is applied. (*See* Kasting Decl., ¶ 17 (Appx A0251).) The subsequent claim language—"wherein the adenosine concentration applied to the dermal cells is [recited amount]"—refers back to, and specifies in numerical terms, the adenosine concentration in the composition that is applied to the skin containing the dermal cells. In other words, the "wherein the adenosine concentration applied to the dermal cells" clause refers to the adenosine concentration in the composition that is applied to dermal-cell-containing skin.

This is confirmed by settled principles of claim interpretation. As the Federal Circuit has explained, "it is a rule of law well established that the definite article 'the' particularizes the subject which it precedes. It is a word of limitation as opposed to the indefinite or generalizing force of 'a' or 'an.'" *NTP, Inc. v. Research in Motion, Ltd.*, 418 F.3d 1282, 1306 (Fed. Cir. 2005), *abrogation on other grounds recognized in Avid Tech., Inc. v. Harmonic Inc.*, 812 F.3d 1040, 1047 (Fed. Cir. 2016). Thus, "the introduction of a new element is accomplished through the use of an indefinite article, not through the use of a definite article." *Tuna Processors, Inc. v. Hawaii Int'l Seafood, Inc.*, 327 F. App'x 204, 210 (Fed. Cir. 2009) (non-

precedential). Here, the claim language uses the indefinite article "a" to introduce the adenosine concentration in the composition. The "wherein" clause, by contrast, uses the definite article "the" when describing the adenosine concentration, thus referring back to the previously identified adenosine concentration in the composition. *See, e.g.*, *Am. Calcar, Inc. v. Am. Honda Motor Co.*, 651 F.3d 1318, 1342 (Fed. Cir. 2011) (explaining that claim language "*prompting a user to select* ***the option*** *to obtain selected information to cope* with the notable condition" referred back to claim phrase "***an option*** is provided").

This understanding is further buttressed by the use of "wherein" to set off this dependent clause. "Wherein" clauses may be used to "relate back to and clarify what is required by the [claim]." *Griffin v. Bertina*, 285 F.3d 1029, 1033-34 (Fed. Cir. 2002). That is precisely the case here: The "wherein" clause of claim 1 relates back to the previously introduced adenosine concentration and clarifies its precise numerical range and that it is applied to skin containing the dermal cells that are the ultimate treatment target.[14] (*See also* Section II.C.3.a-b, *infra*.)

[14] When the patentees used "wherein" clauses to introduce entirely new limitations separate from any antecedent claim element, they did so clearly (*e.g.*, dependent claim 2 ("wherein the composition ***further comprises an angiogenic factor***") and dependent claim 5 ("wherein the composition ***further comprises a conditioning agent***")). In other cases, like the wherein clause at issue here, the clause modifies a previously introduced element (*e.g.*, dependent claim 6 ("wherein ***the*** conditioning agent is a humectant, an emollient, or an occlusive agent")).

The structure of the claims as a whole confirms this understanding. Claim 3 of both patents-in-suit depends from claim 1, and recites "[t]he method of claim 1, wherein the adenosine concentration is 10^{-4} M to 10^{-6} M" ('327 patent) or "10^{-3} M to 10^{-6} M" ('513 patent). Consistent with L'Oréal USA's construction, claim 3 refers to a ***single*** adenosine concentration. By contrast, Plaintiffs' proposed construction renders the dependent claims unintelligible, because it would be unclear whether the dependent claim concentrations refer to the adenosine in the composition or what "reaches the dermal cell layer." *See Wright Medical Tech., Inc. v. Osteonics Corp.*, 122 F.3d 1440, 1445 (Fed. Cir. 1997) ("[W]e must not interpret an independent claim in a way that is inconsistent with a claim which depends from it . . . .").

Plaintiffs' attempt to rewrite the claims is also inconsistent with other portions of the claims. Specifically, Plaintiffs propose to redefine "applied" in the disputed phrase as "reaches." But the claims also recite "topically ***applying*** to the skin a composition comprising a concentration of adenosine," and Plaintiffs do not propose to construe that instance of "apply" as reaches. Nor would it make sense to do so. Plaintiffs' contention that the same word should be construed differently in the same claims therefore contravenes black-letter Federal Circuit law. *See, e.g., Research Plastics, Inc. v. Federal Packaging Corp.*, 421 F.3d 1290, 1295 (Fed. Cir. 2005) ("[C]laim terms are presumed to be used consistently throughout the patent . . . .").

Moreover, in redefining "dermal cells" as "dermal cell ***layer***," Plaintiffs' construction only introduces ambiguity. The phrase "dermal cell layer" appears in neither the claims nor the specification and, to the extent this phrase is even clear, it is distinct from the "dermal cells" themselves. That is because the dermis or dermal cell layer "is composed of a variety of cell types, including fibroblasts" (*i.e.*, a type of dermal cell) as well as extra-cellular material. ('327 patent, 1:19-25; Kasting Decl., ¶¶ 12, 31 (Appx A0245-46, A0259).) Yet Plaintiffs' construction collapses these distinctions, and their attempt to equate the "dermal cell" claim language with a particular layer of the skin also puts the lie to their assertion that the "meaning of 'dermal cells' is dermal cells." (*Supra* at 1, 11.)[15] Such linguistic contortions should be recognized for what they are: an attempt to use *Markman* to reimagine the scope

[15] As explained in the next section, Plaintiffs' redefinition is also contradicted by the specification, which does not use the claim language "applied to the dermal cells" or "reaches the dermal cell layer." Instead, it repeatedly refers to "topically" administering adenosine to "a region of . . . ***skin*** of the mammal ***containing [the] dermal cell***" when discussing the invention. (*See* '327 patent, 1:56-59; *see also id.* at 1:63-66 ("topically administering . . . to a region of skin of the mammal containing the dermal cell"), *id.* at 2:3-6 ("topically administering . . . to a region of skin of the mammal containing the dermal cell").) Plaintiffs' assertion (*supra* at 7-8) that the phrase "skin containing the dermal cells" in L'Oréal USA's construction "merely creates ambiguity and confusion" is thus rebutted by their own patents. And while Plaintiffs now assert that application to the skin is different than application to the dermal cells (*supra* at 12), they contended during the IPRs that the specification discloses that adenosine is "applied [to the dermal cells] by topical routes," *i.e.*, by applying it to the skin. ('327 IPR Patent Owner Preliminary Response at 15 (Appx A0238).)

of the claims to read on products that are clearly not covered, and were in fact expressly distinguished during prosecution.

2. The Specification of the Patents-in-Suit Supports L'Oréal USA's Proposed Construction

The specification further confirms that the recited concentration ranges refer to the adenosine concentration in the composition that is applied to skin containing the dermal cells. The "Summary of the Invention" of the patents-in-suit describes seven categories of "the invention" that are "[b]ased on" the purported discovery that "adenosine stimulates DNA synthesis, increases protein synthesis, and increases cell size in cultures of human skin fibroblasts" contained in the dermis. ('327 patent, 1:36-2:34.) Specifically, the specification refers to: (1) topically administering adenosine to "enhanc[e] the condition of" unbroken skin (1:42-48); (2) topically administering adenosine to promote the healing of broken skin (1:49-53); (3) topically administering adenosine to increase DNA synthesis (1:54-60); (4) topically administering adenosine to increase protein synthesis (1:61-67); (5) topically administering adenosine to increase dermal cell size (2:1-8); (6) culturing fibroblasts "ex vivo" (*i.e.*, out of the body) in adenosine and then reintroducing the fibroblasts to the mammal (2:9-13, hereinafter referred to as "the

isolated fibroblasts embodiment");[16] and (7) a "composition including about 10^{-3} M to about 10^{-7} M adenosine" and an "angiogenesis factor" (2:30-34).

With the exception of the isolated fibroblasts embodiment, each of the above categories involves "topically" administering a "therapeutically effective amount" of adenosine (or an adenosine analog). The specification in turn expressly defines a "therapeutically effective amount" of adenosine as the amount "***applied to the skin***" (*id.* at 2:38-40) in the form of a concentration of "preferably 10^{-3} M to 10^{-7} M, more preferably 10^{-3} M to 10^{-6} M, and most preferably about 10^{-4} M" (*id.*, 2:13-16).[17] The broadest of these concentration ranges is the same as the concentration range recited in independent claim 1 of the '513 patent, while the narrower ranges correspond to ranges from the dependent claims of the patents-in-suit. Likewise, the specification's description of "the invention" as providing "a composition including

[16] Unlike the claims, this procedure does not involve topical application of a "therapeutically effective amount" of adenosine, but instead extracting dermal cells, treating them, and then reintroducing them to the body. (*Id.*; Kasting Decl., ¶ 28 n.4 (Appx A0257).) It therefore does not inform the meaning of the claim language at issue in this case.

[17] While the claims use "amount effective" instead of the term "therapeutically effective amount" in the specification, Applicants explained these two terms are equivalent during prosecution of the parent application. (*See* U.S. Patent Application No. 09/179,006 prosecution history, Mar. 9, 2000 Reply at 3 (Appx A0004) ("Applicant has amended claims 1, 30 and 39 to recite 'effective amount' instead of 'therapeutically effective amount.' This amendment merely deletes an unnecessary word, and does not change the meaning or scope of the claim.").)

about 10^{-3} M to about 10^{-7} M adenosine" confirms that the recited concentration ranges refer to the composition concentration.

In short, the specification, including the "Summary of the Invention," clearly and repeatedly establishes that the alleged topical-application inventions are directed to applying to the skin an adenosine-containing composition in the concentration ranges recited in the "wherein" clauses at issue. *See, e.g.*, *Eon-Net LP v. Flagstar Bancorp*, 653 F.3d 1314, 1322 (Fed. Cir. 2011) ("These statements about the invention are not limited to specific embodiments or examples but describe and define the invention overall.").[18] Tellingly, Plaintiffs ***ignore these "invention" statements in the patents-in-suit*** when discussing the specification (*supra* at 13-14), as they cannot be reconciled with their proposed construction.

Instead, Plaintiffs try to equate the "culturing" of isolated skin fibroblasts described in the "Experimental Information" section with the adenosine concentration that "reaches the dermal cell layer" after topical application. (*Id.*) This argument fails. As noted above, the specification explains that, "[b]ased on" the experimental data work, "the invention provides methods" in which adenosine

[18] *See also Netcraft Corp. v. eBay, Inc.*, 549 F.3d 1394, 1398 (Fed. Cir. 2008) ("[T]he common specification's repeated use of the phrase 'the present invention' describes the invention as a whole . . . ."); *Wireless Protocol Innovations, Inc. v. TCT Mobile, Inc.*, 771 F. App'x 1012, 1018 (Fed. Cir. 2019) (non-precedential) (concluding that "repetition" of particular language "in sections meant to describe the overall invention," including the "Summary of the Invention," supported construing term to have that "requirement").

is "topically appl[ied] . . . to skin" at concentrations of "preferably 10^{-3} M to 10^{-7} M." ('327 patent, 1:37-2:16, 2:38-40.)[19] The only other embodiment described in the Summary of Invention (*i.e.*, the isolated fibroblast embodiment) does not refer to the "therapeutically effective amount" referenced in the "topical[]" application methods. (*Id*. at 2:14-19.) Nor would it make sense to do so, as "therapeutically effective amount" is expressly defined as referring to adenosine concentrations that are "applied ***to the skin***." ('327 patent, 2:14-16, 38-40.) The Experimental Information section, by contrast, discloses only "culturing" the fibroblasts with, or "expos[ing]" them to—as opposed to "applying"—adenosine. ('327 patent, 7:50-53, 7:64-65, 8:26-29, 8:52-54, 8:61-64); *see also, e.g.*, *supra* at 9-10 (quoting the Board and characterizing these experiments as involving adenosine "applied ***directly*** to dermal cells (fibroblasts)")[20].)

Consistent with the above, the specification also nowhere describes topically applying a first identified concentration of adenosine that results in a second

[19] For this reason, that topically applied adenosine concentrations may reach the dermis and the assertion that certain formulation components may enhance skin penetration (*see* '327 patent, 5:12-24; *supra* at 13-14; '327 IPR Patent Owner Preliminary Response at 15 (Appx A0238)) say nothing about whether the recited concentration range "reaches the dermal cell layer."

[20] The distinction between "applied ***directly***" and "applied" generally is consistent with "'apply'" being defined as "'to bring into physical contact with ***or close proximity to***.'" (*Supra* at 13 (quoting '327 IPR Rehearing Decision).) L'Oréal USA notes that the Board also failed to analyze the "or close proximity to" aspect of the dictionary definition it quoted, including in light of the specification's disclosure.

identified concentration at the dermal cell layer.[21] And the patents-in-suit are entirely silent on how the precise concentration of adenosine at the dermal cell layer would be determined, or whether that is even possible. In any event, a person of ordinary skill in the art would understand these experiments at most to show that certain activity occurs in *in vitro* fibroblasts when exposed to adenosine at 10^{-4} M to 10^{-6} M and that, when applied topically, compositions containing the claimed adenosine concentrations could lead to those results. (Kasting Decl. ¶ 29 (Appx A0257-58).)[22]

3. L'Oréal USA's Proposed Construction Is Confirmed by the Prosecution History

The prosecution history—specifically (1) the history of the pertinent claim language, (2) Applicants' repeated, consistent statements describing the claimed subject matter and prior art, and (3) the Examiner's expressed understanding of the claim language—only further confirms L'Oréal USA's construction. *See, e.g.*,

[21] Plaintiffs' proposed construction also defies logic, as it would allow the patentees to simultaneously contend that their putative invention covers the same concentration ranges when topically applied and at the dermal cells following topical application, even though the specification states that certain amounts of the composition will not penetrate through the skin. ('327 patent, 5:12-24 (explaining that penetration needs to "be enhanced"); Kasting Decl., ¶¶ 17, 30 & n.6 (Appx A0251, A0258-59).)

[22] In this regard, it bears noting that the upper bound of the claimed concentration range of the '513 patent and the specification's "prefer[red]" upper bound for topical concentrations is 10^{-3} M (*i.e.*, a 10-times-greater concentration of adenosine than the 10^{-4} M used in the isolated fibroblast experiments).

Phillips, 415 F.3d at 1317 (explaining that "a court should also consider the patent's prosecution history," which "provides evidence of how the PTO and the inventor understood the patent"); *Desper Products, Inc. v. QSound Labs, Inc.*, 157 F.3d 1325, 1336-37 (Fed. Cir. 1998) ("Prosecution history is an important source of intrinsic evidence in interpreting claims because it is a contemporaneous exchange between the applicant and the examiner."). Moreover, the prosecution history is "especially important" where, as here, "there is particular prior art that the applicant is trying to distinguish." *Engel Indus., Inc. v. Lockformer Co.*, 96 F.3d 1398, 1405 (Fed. Cir. 1996).

As explained below, throughout prosecution, Applicants characterized—and the PTO understood—their alleged invention to be directed to particular adenosine concentrations in compositions to be topically applied to the skin.[23]

[23] The Board, as well as Plaintiffs' opening brief, attempts to dismiss this evidence as not rising to the level of disclaimer (*e.g.*, *supra* at 15, 17-19; '327 IPR Decision at 11-13 (Appx A0182-84); '327 IPR Rehearing Decision at 7-10 (Appx A0219-22)), but even if that were true (it is not), it is of no moment. A patent's prosecution history is relevant not only to ascertaining potential disclaimers, but as evidence of ordinary meaning. *See, e.g.*, *Medrad, Inc. v. MRI Devices Corp.*, 401 F.3d 1313, 1319 (Fed. Cir. 2005) ("We cannot look at the ordinary meaning of the term in a vacuum. Rather, we must look at the ordinary meaning in the context of the written description and the prosecution history."); *Shire Dev., LLC v. Watson Pharm., Inc.*, 787 F.3d 1359, 1366 (Fed. Cir. 2015) (explaining that prosecution history statements "do inform the claim construction," even when they "do not rise to the level of unmistakable disavowal"). Regardless, this evidence rises to the level of a clear and unmistakable disclaimer. *See, e.g.*, *Biogen Idec, Inc. v. GlaxoSmithKline LLC*, 713 F.3d 1090, 1096-97 (Fed. Cir. 2013).

a. The Prosecution Leading to the ’327 Patent

When the predecessor to what would ultimately become claim 1 of the ’327 patent was first introduced, the claim was explicit that the recited adenosine concentration referred to the concentration in the composition—consistent with the discussion of the invention in the specification. Original claims 70 and 72, as first presented to the PTO, are reproduced below:

> 70. A method for enhancing the condition of unbroken skin of a mammal by reducing one or more of wrinkling, roughness, dryness, or laxity of the skin, without increasing dermal cell proliferation, the method comprising topically applying to the skin a composition ***comprising a concentration of adenosine*** in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation.
>
> 72. The method of claim 70, where in ***the adenosine concentration*** is 10^{-4} M to 10^{-6} M.

(’327 prosecution history at 62 (Appx A0058).)

Per the above language, the adenosine concentration, including the numerical range, refers to the concentration in the composition being applied to the skin. And there is no suggestion that this refers to any concentration that “reaches the dermal cell layer.” Instead, as Applicants explained, “Claim 70 covers a method for enhancing the condition of unbroken skin . . . ***by topically applying to the skin a composition comprising a concentration of adenosine***, but not adenosine analogs, in an amount effective to enhance the condition of the skin without increasing cell

proliferation." (*Id.* at 65-66 (Appx A0061-62).) Applicants further explained that "claims to specific concentrations are supported by the original claims and in the application, e.g., at page 3, lines 15-18." (*Id.* at 63 (Appx A0059).) Page 3, lines 15-18 of the specification, in turn, states: "The therapeutically effective amount of adenosine used in the above-described methods [*i.e.*, all of the "topically administered" methods, as explained above] is preferably 10^{-3} M to 10^{-7} M, more preferably 10^{-4} M to 10^{-6} M, and most preferably about 10^{-4}M." (*Id.* at 12 (Appx A0031); '327 patent, 2:13-17; '513 patent, 2:19-23.)

Claim 1 of the '327 patent took its final form following an amendment to overcome a prior art rejection. ('327 prosecution history at 81 (Appx A0075).) Specifically, Applicants added the language "wherein the adenosine concentration applied to the dermal cells is 10^{-4} M to 10^{-7} M" to what was then-pending claim 70 shown above. (*Id.* at 81, 88 (Appx A0075, A0082).) Despite the inclusion of the heretofore-unused term "applied to the dermal cells," Applicants made clear that "[t]his amendment would ***add no new matter***, as it merely includes a range of concentrations of adenosine recited in the dependent claims and in the specification at page 3, lines 15-18." (*Id.* at 82 (Appx A0076).) Thus, no new concepts were introduced to the claims, including a different adenosine concentration that "reaches" the dermal cell layer. And, in explaining this amendment, Applicants never referred to direct topical application of the dermal cells, or any specific

concentration of adenosine that "reaches" the dermal cells. Instead, Applicants explained that claims 70 to 79 "are based on the ***application*** of certain concentrations of adenosine ***to the skin*** to achieve certain results" (*id.*), consistent with the meaning of the cited specification passage (*see* Section II.C.2, *supra*).[24]

At the same time, Applicants relied on this recited concentration range in an attempt to overcome prior art ("Hartzshtark" and "DE107") that disclosed using adenosine to improve skin condition in concentrations that correspond to the concentrations of the L'Oréal USA products accused of infringement in this case. Specifically, Hartzshtark disclosed that a 0.1% adenosine composition was effective in treating skin. (Hartzshtark at 378-79 (Appx A0291-92); Kasting Decl., ¶ 20 (Appx A0253).) Similarly, DE107 disclosed the use of compositions containing at least 0.001% adenosine by weight, and included six enumerated examples having 0.1% adenosine. ('327 prosecution history at 97, 103-106 (Appx A0085, A0091-94); Kasting Decl., ¶ 19 (Appx A0252); *see also id.* at ¶ 16 (Appx A0247-50).) In both cases, Applicants made apples-to-apples statements comparing the prior art concentrations with the concentrations recited by the claims, and did not discuss the concentration of adenosine that "reaches" the dermal cells in attempting to

[24] To interpret the claims otherwise, as Plaintiffs now propose, would be to impermissibly introduce new matter by amendment that is not described in the specification—namely, the topical application of adenosine to unbroken skin that results in adenosine that "reaches" the dermal cell layer at the recited concentrations—and invalidate the claims under 35 U.S.C. § 112.

distinguish this prior art. (*See* '327 prosecution history at 81-87 (Appx A0075-81).)[25]

With respect to Hartzshtark, Applicants acknowledged that "Hartzshtark indicates in the Table on page 379 that the adenosine concentration effective to reduce [skin] indentation was 0.1% (3.8×10^{-3} M)," but argued, *inter alia*, that "[t]he proposed amended ***claims would recite a maximum concentration of adenosine of 10^{-4} M***." (*Id.* at 85 (Appx A0079).) "***Thus***," according to Applicants, "Hartzshtark does not anticipate claim 70 as amended." (*Id.*) Tellingly, Plaintiffs also ignore these statements in their opening brief, and the Board did not address them during the IPR proceedings.

With respect to DE107, Applicants stated that DE107's disclosure of 0.001% adenosine "corresponds to 3.8×10^{-5} M adenosine," and then acknowledged that "***[t]his is between the 10^{-4} M and 10^{-5} M concentrations recited in the claims of the present application***." (*Id.* at 84 (Appx A0078).) Applicants also stated that "[o]ther sections of [DE107] recite higher concentrations for a lower limit of adenosine," and described the examples as disclosing "a relatively high concentration of 0.1%

[25] These statements were reiterated by the named inventors in a declaration submitted to the PTO that included much of the same language in Applicants' response to the office action. (*See* '327 prosecution history at 107-111 (Appx A0095-99).)

adenosine."[26] (*Id.*) Not surprisingly, these statements also go unmentioned in Plaintiffs' opening brief, which cites only other arguments Applicants made. (*Supra* at 16-19.) But any such ***additional*** arguments do not alter the clear import of the above.[27] *See, e.g.*, *Amgen Inc. v. Coherus Biosciences, Inc.*, 931 F.3d 1154, 1159-60 (Fed. Cir. 2019) (holding that, "[w]here a patent applicant sets forth multiple bases to distinguish between its invention and the cited prior art," each of the "separate arguments" is relevant to claim scope, regardless of "whether or not [it was] actually required to secure allowance of the claim").

Applicants also argued, with respect to both references, that "there would have been no suggestion or motivation in any of the cited references for one of skill in this field to use **a maximum** concentration of 10^{-4} M adenosine as recited in Applicants' claim 70." (*Id.* at 86 (Appx A0080) (emphasis in original).) All of these statements concerning multiple prior art references further confirm that the disputed claim term—consistent with the claim language as a whole and the specification—

[26] Indeed, the Board acknowledged that these statements "provide some support" for L'Oréal USA's position, but (1) improperly focused on only one of them and (2) viewed them only through the lens of prosecution history disclaimer, and thus improperly discounted the significance of Applicants' repeated and consistent statements. ('327 IPR Decision at 11-13 (Appx A0182-84); '327 IPR Rehearing Decision at 7-10 (Appx A0219-22).)

[27] Contrary to Plaintiffs' apparent suggestion (*supra* at 17), the quoted statement from the "PTO" did ***not*** occur during prosecution, but instead was made by the Board in its denial of rehearing. As explained below, there can be no debate that the PTO during prosecution understood the claims to refer to application to the skin.

refers to the adenosine concentrations in compositions applied to the skin, and cannot be squared with Plaintiffs' litigation position that the same concentrations distinguished during prosecution can somehow now infringe the patents-in-suit.[28]

Consistent with the foregoing, in allowing the claims, the PTO stated that the "[i]nstant claims are directed to . . . ***administering*** adenosine at a ***concentration of 10^{-4} to 10^{-7} M to the skin***. The ***prior art*** of record teaches administering adenosine to skin for treating aging. However, the art of record utilizes ***concentrations much higher than claimed*** . . . ." (*Id.* at 117 (Appx A0101).) Both the PTO and Applicants therefore understood the claimed concentration range to refer to the concentration of adenosine applied "to the skin," and the PTO memorialized this understanding in the Reasons for Allowance. *See, e.g.*, *ACCO Brands, Inc. v. Micro Sec. Devices, Inc.*, 346 F.3d 1075, 1079 (Fed. Cir. 2003) ("We conclude that the pin clause of claim 10 must be construed in the same way as the pin clause of claim 1, for the examiner's Reasons for Allowance make clear that the examiner and the applicant understood

[28] For this reason, Plaintiffs' argument that these statements were made "only to show 'the extremely broad range of adenosine concentrations'" in one of the prior art references, and that both references "taught 'the use of adenosine for increasing cell proliferation,'" are misplaced. (*Supra* at 16-19.) Indeed, the portion of the prosecution history cited for the latter statement does not even mention Hartzshtark ('327 prosecution history at 84 (Appx A0078)), and Hartzshtark does not discuss cell proliferation at all. (Hartzshtark at 378-79 (Appx A0291-92); Kasting Decl., ¶ 20 (Appx A0253).)

that the invention requires that the pin extends (actively) into the slot after rotation.").

Plaintiffs attempt to erase the clear import of the above by citing Applicants' "Comments on Statement of Reasons for Allowance," arguing that the "inventors responded with comments on May 17, 2002, clarifying that the recited concentration is not administered 'to the skin.'" (*Supra* at 15 (emphasis in original).) Applicants said no such thing, nor did they in any way disagree with the Examiner. Rather, they stated that "the claims are allowable for at least all of the reasons of record in Applicants' responses, and Applicants do not concede that the Examiner's Statement of Reasons for Allowance ***is the only reason for which claims 70 to 79 are allowable***"—thereby actually ***agreeing*** with the Examiner's position. ('327 prosecution history at 123 (Appx A0103).) Applicants also parroted back the claim language by "not[ing] that the claimed concentration of adenosine is applied to the dermal cells." (*Id*.) Applicants did not explain what they meant by this, or how it differed, if at all, from the clear understanding demonstrated by Applicants and the PTO during prosecution (a notable omission given the position Plaintiffs are now advancing). Regardless, Applicants' comments "do[] not, [and] indeed cannot,

change the examiner's Reasons for Allowance." *E.g.*, *Biogen, Inc. v. Berlex Labs., Inc.*, 318 F. 3d 1132, 1139 (Fed. Cir. 2003).[29]

b. The Prosecution Leading to the '513 Patent

Like the prosecution history of the parent '327 patent, the '513 patent prosecution history confirms that Applicants' purported invention relates to topically applying certain adenosine concentrations. What would become claims 1, 3, and 4 of the '513 patent were first introduced by amendment as original claims 54, 56, and 57. They read, as they do in their final form, as follows:

> 54. A method for enhancing the condition of unbroken skin of a mammal by reducing one or more of wrinkling, roughness, dryness, or laxity of the skin, without increasing dermal cell proliferation, the method comprising topically applying to the skin a composition comprising a concentration of adenosine in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, wherein the adenosine concentration applied to the dermal cells is 10^{-3} M to 10^{-7} M.
>
> 56. The method of claim 54, wherein the adenosine concentration is 10^{-3} M to 10^{-6} M.
>
> 57. The method of claim 54, wherein the adenosine concentration is about 10^{-3} M.

In explaining this amendment, Applicants stated:

[29] Plaintiffs rely on the Board in connection with this point (*supra* at 15-16), but its statement that "Patent Owner expressly corrected the Examiner" was clearly wrong as a matter of fact and overlooked the Federal Circuit case law cited above.

> All of these new claims are supported by the claims filed in the original application. For example, new independent claim 54 is supported by original claims 1 and 8. The recitation of specific concentrations of adenosine in claims 54, 56, and 57 are supported by the original claims and in the application, e.g., at page 3, lines 15-18.

('513 prosecution history at 62, 64 (Appx A0134, A0136).)

As explained above, the original application does not describe topically applying a composition containing adenosine to unbroken skin where a separately specified adenosine concentration "reaches" the dermal cells (or the "dermal cell layer"). Likewise, original claim 1, and dependent claim 8, and page 3, lines 15-18 of the application as filed concern the concentration of adenosine that is applied topically to the skin. (*See id*. at 30 (Appx A0127) (original claim 1, reciting, in relevant part, "[a] method for enhancing the condition of non-diseased skin of a mammal, comprising ***topically applying*** a therapeutically effective amount of a composition comprising adenosine or an adenosine agonist ***to non-diseased skin of said mammal***"), *id.* at 12 (Appx A0109) (explaining that "[t]he therapeutically effective amount of adenosine used in the above-described methods is preferably 10^{-3} M to 10^{-7} M, more preferably 10^{-4} M to 10^{-6} M, and most preferably about 10^{-4} M").) And Applicants never stated or suggested during prosecution that the cited claims or specification passage referred to an adenosine concentration that "reaches" the dermal cell layer.

Rather, Applicants confirmed that "wherein the adenosine concentration applied to the dermal cells is 10^{-3} M to 10^{-7} M" refers to the concentration that is applied to the skin when comparing the claims to the prior art. For example, in arguing nonobviousness over the prior-art "von Borstel patent," Applicants stated: "One of skill in the art would not have thought to use adenosine based on the von Borstel patent, ***much less known what amount to apply to skin.***" (*Id*. at 67 (Appx A0139).) Thus, consistent with L'Oréal USA's construction and the intrinsic record as a whole, Applicants again focused on the concentration of adenosine to be applied to the skin.

As with the '327 patent, the Notice of Allowance for the '513 patent confirms this understanding. Following the above arguments, the PTO stated in allowing the claims:

> Instant claims are directed to a method of . . . ***administering adenosine at a concentration of 10^{-3} M to 10^{-7} M, to the skin***. The closest prior art of record teaches administering adenosine in skin care compositions. However, ***the art of record utilizes concentrations much higher than claimed*** . . . . Further, prior art of record does not teach or suggest any reason for the addition of adenosine in skin care compositions, in particular, ***in amounts as low as those claimed.***

(*Id*. at 74 (Appx A0143).) In responding to this Notice of Allowance, which mirrors that in the '327 patent prosecution, Applicants once again did not identify any errors, but instead ***agreed*** with the Examiner's reasons: "Applicants submit that in addition

to the reasons stated by the Examiner in the Notice of Allowability mailed April 22, 2003, claims 54 to 63 are allowable for the reasons of record in this application." (*Id.* at 83 (Appx A0145).) Applicants did not include the alleged "correction" on which Plaintiffs (and the Board) so heavily rely. (*Id.*)

The '513 patent's prosecution history and Reasons for Allowance, which are unaddressed in both Plaintiffs' brief and the Board's decisions (*see, e.g.*, '513 IPR Decision at 10-12 (Appx A0202-04); '513 IPR Rehearing Decision at 7-10 (Appx A0231-34).), provide further compelling evidence that the disputed claim language refers to the concentration that is applied to the skin. *See, e.g.*, *ACCO Brands*, 346 F.3d at 1079.

c. The Prosecution of Related Patent Applications

The prosecution history of subsequent, related patent applications from the same family may also be used to inform the interpretation of disputed claim language. *See, e.g.*, *MasterMine Software, Inc. v. Microsoft Corp.*, 874 F.3d 1307, 1311 n.2 (Fed. Cir. 2017) ("We have often held that the meaning of claim terms in one patent can be informed by statements made during prosecution of other patents in the same family. We have explained, for example, that past and future prosecution of related patents may be relevant to the construction of a given claim term."). Could there be any doubt (there is none), the prosecution of U.S. Patent Application No. 10/680,370 ("the '370 application") from the same patent family further

confirms that the concentration ranges in the asserted claims refer to the concentration in the composition, and not the concentration that "reaches the dermal cell layer."

During prosecution of the '370 application, Applicants introduced original claim 54, which recited:

> A method for enhancing the condition of unbroken skin of a mammal by reducing one or more of wrinkling, roughness, dryness, or laxity of the skin without increasing proliferation of dermal cells in the skin, the method comprising ***topically applying to the skin*** a composition comprising ***a concentration of an adenosine analog*** in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, ***wherein the adenosine analog concentration applied to the dermal cells is about 10^{-4} M to 10^{-7} M***.

('370 application prosecution history, June 8, 2005 Reply at 2 (Appx A0148).) In arguing that a particular prior art reference ("the '649 patent") that disclosed the use of adenosine triphosphate ("ATP," an adenosine analog) was not anticipatory, Applicants stated:

> More importantly, the '649 patent does not disclose the same concentrations of ATP as recited in applicants' amended claims to the use of adenosine analogs. The '649 patent recites percentages of ATP of 0.045 to 4.5 percent by weight ***of the composition***. Given ATP's molecular weight, this concentration range is far higher than applicants' claimed range of concentrations. Applicants' highest claimed concentration is now 10^{-4} M, which corresponds to an ATP concentration of about 0.006 percent. This upper concentration of 0.006 percent is far

> lower that [*sic*] the 0.045 percent lower level that the '649 patent discloses . . . .

(*Id*. at 7 (Appx A0153).) That is, Applicants yet again made an apples-to-apples comparison of the concentration of prior-art compositions with claimed concentrations expressed as being "applied to the dermal cells." In so doing, Applicants once again confirmed what the claims and specification already make plain: The adenosine concentrations in the claims are those that are applied to the skin containing the dermal cells.

The PTO confirmed this understanding in a subsequent office action rejecting the pending claims of the '370 application over certain claims of the '513 patent for obviousness-type double patenting. Specifically, the PTO stated:

> [The conflicting claims] are not patentably distinct from each other because both the sets of claims are directed to a method of enhancing the skin condition by topically applying adenosine or adenosine analog in an amount effective to enhance the condition of the skin. The patented claims recite ***the effective amount of adenosine*** [*i.e.*, which the claims of the '513 patent specify is applied to the skin] or its analogs ***between 10^{-3} to 10^{-7} M***. The application claims recite the amount of adenosine analog from 10^{-4} to 10^{-7}, which falls within the claimed range of the patent[].

('370 application prosecution history, Final Rejection at 3 (Appx A0159).) As is clear from the above, the PTO understood both the pending claims and the asserted '513 patent claims to refer to topically applying an effective amount of adenosine (or an analog thereof), where the concentration applied to the skin is the recited

numerical amount.[30] Importantly, there was once again no mention by Applicants of the "reaches the dermal cell layer" fiction that they have now created in an attempt to justify bringing a baseless litigation.

* * *

In sum, consistent with the claim language itself and the specification, throughout the prosecution of the patents-in-suit and related applications, Applicants made clear that the claims are directed to the adenosine concentrations applied to the skin. Plaintiffs should not now be permitted to change course in an attempt to manufacture infringement claims against products containing the ***very same*** concentrations distinguished during prosecution. *See, e.g.*, *Southwall Techs., Inc. v. Cardinal IG Co.*, 54 F.3d 1570, 1576 (Fed. Cir. 1995) ("Claims may not be construed one way in order to obtain their allowance and in a different way against accused infringers."); *01 Communique Lab., Inc. v. Citrix Sys., Inc.*, 889 F.3d 735, 743 (Fed. Cir. 2018) ("A patent may not, like a nose of wax, be twisted one way to avoid anticipation and another to find infringement."). Because L'Oréal USA's construction is the one that "stays true to the claim language and most naturally

[30] Lest any doubt remains, the PTO went on to reject the claims again, relying on prior art that disclosed adenosine analog concentrations in the compositions. ('370 application prosecution history, Final Rejection at 4-9 (Appx A0160-65) ("[The] '423 [patent] discloses various formulations of the composition . . . . Furthermore, the '423 patent disclosed that the concentration could typically be in the range from about 0.001% to 20% . . . .").)

aligns with the patent's description of the invention," it should be adopted.[31] *See, e.g.*, *Phillips*, 415 F.3d at 1316 ("Ultimately, the interpretation to be given a term can only be determined and confirmed with a full understanding of what the inventors actually invented and intended to envelop with the claim.").

III. PLAINTIFFS' REPLY POSITION

It is undisputed that "the skin" is composed of multiple layers, both the epidermis and the dermis below it, which are separate layers of the skin. Defendant seeks to rewrite the claim language such that the recited numerical "concentration" of adenosine is not "applied to the dermal cells," as the claims require, but instead is "applied to the skin." In other words, Defendant argues the claims broadly cover application of the recited concentration of adenosine to any part of the skin, such as the upper, epidermal layer of the skin, even though the claims plainly limit application of the recited concentration to "the dermal cells." For the reasons explained in Plaintiffs' opening brief, and further below, the intrinsic evidence unambiguously supports Plaintiffs' plain and ordinary construction. Defendant's construction should be rejected.

[31] As explained above, the prosecution history, along with the rest of the intrinsic record, supports L'Oréal USA's ordinary-meaning construction of the disputed claim term. To the extent there is any ambiguity on this point, however, the prosecution history statements described above also amount to a clear and unmistakable disclaimer of compositions having adenosine concentrations above 10^{-3} M. *See, e.g.*, *Biogen Idec*, 713 F.3d at 1096-97.

1. The PTO Correctly Decided This Dispute Long Ago

In an attempt to convince this Court to order a contrived construction that conflicts with the intrinsic evidence, Defendant repeats its arguments that the PTO rejected approximately a year and a half ago in four separate written decisions.

Defendant purports to present a new construction to this Court, claiming that the PTO "focused extensively on the difference between the epidermis and dermis," but that is "not the focus of the present dispute, which centers on the meaning of the word 'applied.'" Opp. at 25-26 n.10. But Defendant's proffered meaning of the word "applied" is that the claimed numerical concentration of adenosine is the amount in the composition itself and is therefore applied to the top, epidermal layer of skin, rather than the amount that is "applied to the dermal cells," as the claims actually state. *See, e.g.* Opp. at 22-23, 27-28. That is precisely the argument Defendant made to the PTO. *See* '327 IPR Denial at 9 (App'x A0180) ("The fundamental question presented by [Defendant] in connection with its proposed construction is whether the recited concentration [of adenosine] is applied to the dermal cells or the epidermal cells."). After carefully considering the same evidence Defendant presents now again, the PTO concluded "the disputed claim language is unambiguous [and] requires an adenosine concentration 'applied to the dermal cells.'" *Id.* at 6, 15 (App'x A0177, A0186).

Defendant argues the PTO's decision is somehow unreliable because the PTO was not aware of Plaintiffs' position that their patented technology is infringed by a vast array of Defendant's products. Plaintiffs' infringement contentions are irrelevant to the present dispute, because "[i]t is well settled that claims may not be construed by reference to the accused device." *NeoMagic Corp. v. Trident Microsystems, Inc.*, 287 F.3d 1062, 1074 (Fed. Cir. 2002); *see also StrikeForce Techs., Inc. v. PhoneFactor, Inc.*, No. CIV.A. 13-490-RGA, 2015 WL 3793726, at *5 n.49 (D. Del. May 26, 2015) ("[C]laim construction focuses on the patent, not the products accused of infringement."). *Wilson Sporting Goods Co. v. Hillerich & Bradsby*, 442 F.3d 1322 (Fed. Cir. 2006), does not hold otherwise. *See Fitness Anywhere LLC v. Woss Enters. LLC*, No. 14-CV-01725-BLF, 2015 WL 7293659, at *5 n.3 (N.D. Cal. Nov. 19, 2015) ("*Wilson* does not compel the Court to consider the accused products in construing claims in a claim construction hearing. *Wilson* only suggests that 'if the litigants cannot themselves inform a trial court of the specific issues presented by the infringement inquiry . . . then a trial court may refer to the accused product or process for that context during the process.' Accordingly, the Court DENIES [Defendant's] request to consider the accused products in construing the claims.") (quoting *Wilson*, 442 F.3d at 1331).

Nor is it even clear what Defendant believes the import is of Plaintiffs' infringement contentions. The fact that Defendant admits that its products infringe

the technology disclosed by certain prior art is immaterial to whether its products also infringe the novel technology disclosed by Plaintiffs' patents. *See*, *e.g.*, '327 IPR Denial at 15-17 (App'x A0186-88) (DE '107 does not anticipate or render obvious the asserted patents because there is no evidence in DE '107 "reflecting the concentration of adenosine applied to the dermal cells"). Moreover, the PTO did know that Defendant filed its IPR petition after Plaintiffs filed suit, alleging that Defendant infringes the asserted patents.

In any event, Plaintiffs' infringement contentions in this case reflect exactly what it represented to the PTO and the PTO decided: "adenosine is first topically applied to the epidermal layer of the skin and, only after it penetrates this outer skin layer, is a specific concentration (10^{-4} M to 10^{-7} M)[32] of the adenosine 'applied' to the dermal cells." '327 Reconsideration Denial at 6 (App'x A0218). Because using many of Defendant's products meets these limitations, they infringe the asserted patents. Indeed, Plaintiffs have alleged that Defendant willfully took Plaintiffs' technology, based on discussions between the Parties and Defendant's own patent filings. *See* D.I. 13 (First Amended Complaint) ¶¶ 19-30.

2. The Intrinsic Evidence Compels a Plain and Ordinary Meaning Construction

[32] For the '513 Patent, 10^{-3} M to 10^{-7} M.

The Parties agree that "the skin" is composed of multiple layers, including the epidermis and the dermis, which are separate layers of the skin. *See, e.g.*, Kasting Dec. ¶ 10 (App'x A0244-45). And the Parties agree that the dermis, which contains dermal fibroblasts, is beneath the epidermis. *See, e.g. id.* ¶ 12 (App'x A0245-46). Similarly, it is undisputed that when a composition is applied "topically," it is applied to the top, epidermal layer of skin, and only a portion of that composition "permeates to a particular layer within the skin," such as the dermis. *Id.* ¶¶ 14, 17 (App'x A0246-47, A0251). The claims at issue teach applying a specified concentration of adenosine "to the dermal cells," and the only dispute between the parties is whether the claimed adenosine concentration must be applied "to the dermal cells," like the claims say, or if it is applied to some other part of "the skin," such as to the epidermis. The Federal Circuit imposes a "heavy presumption that a claim term carries its ordinary and customary meaning." *CCS Fitness, Inc. v. Brunswick Corp.*, 288 F.3d 1359, 1366 (Fed. Cir. 2002) (citations and quotations omitted). Defendant claims it seeks an "ordinary-meaning construction," Opp. at 22, but only Plaintiffs have requested the Court to order this term has its plain and ordinary meaning. *See* D.I. 77. In contrast, Defendant seeks to add new language to the claim, replacing the limitation "the dermal cells" from the patent claims with some other area of "the skin." As explained in Plaintiffs' opening brief, and further

below, Defendant cannot meet its "heavy" burden to support a construction that erases a critical claim limitation and conflicts with the intrinsic evidence.

The Claim Language

Claim 1 of each asserted patent recites a "method comprising topically applying to the skin a composition comprising a concentration of adenosine in an amount effective to enhance the condition of the skin without increasing dermal cell proliferation, wherein the adenosine concentration applied to the dermal cells is" either 10^{-4} M to 10^{-7} M, for the '327 Patent, or 10^{-3} M to 10^{-7} M for the '513 Patent. Thus, the claim language twice refers to a "concentration" of adenosine and contrasts the different skin structures the concentration may be "applied" to: a "composition comprising a concentration of adenosine" is "topically applied to the skin," and "the adenosine concentration" is "applied to the dermal cells" in a specific numerical range.

"In the patent claim context the term 'comprising' is well understood to mean 'including but not limited to.'" *CIAS, Inc. v. All. Gaming Corp.*, 504 F.3d 1356, 1360 (Fed. Cir. 2007) (discussing cases). Because the "composition" includes, but is not limited to, the recited adenosine concentration, it may also include other ingredients, such as more adenosine that is not ultimately "applied to the dermal cells." *See* Kasting Dec. ¶ 17 (App'x A0251) (opining that only a portion of a topically applied composition "permeates to a particular layer within the skin"). The claims disclose

a numerical range for only the adenosine that is "applied to the dermal cells," and not the amount of adenosine that is in the "composition" itself, except to say that the composition includes, but is not limited to, the amount of adenosine in the concentration that is "applied to the dermal cells." The claims are directed to what amount of adenosine will be applied to, and thus affect, the dermal cells.

Had the inventors intended the "composition comprising a concentration of adenosine" to include the identical amount of adenosine as what is "applied to the dermal cells," they easily could have said so. They did not, instead carefully contrasting "the skin" and "the dermal cells," requiring the recited numerical concentration of adenosine to be "applied to the dermal cells." *See, e.g.*, '327 Reconsideration Denial at 6 (App'x A0218) ("In this context, the meaning of claim 1 is clear: adenosine is first topically applied to the epidermal layer of the skin and, only after it penetrates this outer skin layer, is a specific concentration (10^{-4} M to 10^{-7} M) of the adenosine 'applied' to the dermal cells.").

According to Defendant, because the claim language provides only one numerical range of adenosine (the "concentration"), but recites that the concentration will be "applied" to "the skin" (as part of the "composition") as well as "the dermal cells" (a layer of the skin), the claims equate the skin and the dermal cells. Defendant's argument defies logic. The claims disclose one numerical concentration of adenosine, which is "applied to the dermal cells." The composition

applied "to the skin" need not be limited to only the recited adenosine concentration. Indeed, as Defendant recognizes, it often will not contain the same amount because not all adenosine will necessarily penetrate to the dermal layer. *See* Kasting Dec. ¶ 17 (App'x A0251). Instead, the concentration applied "to the skin" includes the amount of adenosine that penetrates to the dermal cells, as well as other ingredients, such as more adenosine, that may not penetrate to the dermal cells. And the claim then specifies the range of the concentration "applied to the dermal cells."

Defendant also argues Plaintiffs' plain and ordinary meaning construction would render the dependent claims "unintelligible," where a number of them refer to a concentration of adenosine, and a POSITA would be unable to understand which concentration of adenosine they refer to under Plaintiffs' construction. Defendant's argument falls flat. There is only one numerical range of adenosine in the independent claims, which the dependent claims refer back to. As explained above, Defendant misconstrues the "composition comprising a concentration of adenosine" as a composition that is limited to the recited concentration of adenosine, instead of a composition that includes the recited concentration of adenosine. *But see CIAS*, 504 F.3d at 1360. In fact, Defendant's construction renders the dependent claims unintelligible. Dependent claim 9 of both patents, which discloses a "transdermal delivery agent," would make no sense if the claims did not teach penetration of adenosine to the dermis.

The Specification

The specification explains that a composition containing adenosine should be topically applied to the skin, and the adenosine will "penetrate" into the skin. *See* Opening Br. at 13-14 (quoting the '327 Patent at 5:10-25). Moreover, the inventors disclosed experiments in the specification in which adenosine of an amount within the claimed ranges was applied directly to dermal fibroblast cells to demonstrate its effect, confirming they intended the claimed range of adenosine to be applied to the dermal cells. *See id*.

Defendant argues that because the specification discusses applying a "therapeutically effective amount" of adenosine "topically" or to "the skin," and equates a "therapeutically effective amount of adenosine" with the claimed ranges of adenosine, the recited concentration of adenosine must be the amount of adenosine in the composition itself, which is applied to the epidermis. Defendant's argument again misapprehends the basic logic of the patents: a composition that includes but is not limited to the claimed range of adenosine is applied topically, some portion of the composition penetrates, *see* '327 Patent at 5:10-25; Kasting Dec. ¶ 17 (App'x A0251), and thus the disclosed concentration of adenosine is applied to the dermal cells. As the PTO stated in denying Defendant's Request for Reconsideration, "[i]n this context, the meaning of claim 1 is clear: adenosine is first topically applied to the epidermal layer of the skin and, only after it penetrates this

outer skin layer, is a specific concentration (10^{-4} M to 10^{-7} M) of the adenosine 'applied' to the dermal cells." *See* '327 Reconsideration Denial at 6 (App'x A0218).

Defendant suggests the scientific experiments described in the specification somehow undermine the plain language of the claims. In the specification, the inventors disclosed "[e]xperimental [i]nformation," '327 Patent at 6:15, in which adenosine within the claimed range (10^{-4} M) was applied directly to dermal fibroblasts, which "suggest[s] that the inventors considered it desirable for the dermal cells to receive the claimed concentration of adenosine." '327 Reconsideration Denial at 5-6 (App'x A0217-18). Defendant inexplicably characterizes this section of the specification as disclosing an "embodiment" that, according to Defendant, is irrelevant because it does not call for topical application of adenosine. But the specification's discussion of the inventors' experiments, demonstrating "the effect of adenosine" in the claimed ranges on, for example, "DNA synthesis," "protein synthesis," or "cell size," *see* '327 Patent at 7:59; 8:49; 8:59, is not an embodiment of the patented method, but a description of its results, *see id.* at 1:38-42 ("We have discovered that adenosine stimulates DNA synthesis, increases protein synthesis, and increases cell size in cultures of human skin fibroblasts. Based on this discovery, the invention provides methods for enhancing the condition of skin."); *cf. Autogiro Co. of Am. v. United States*, 384 F.2d 391, 409 (Ct. Cl. 1967) ("The conjoint operation of rotor drive and pitch change controls to

effect a vertical take-off is not an embodiment of the invention, but is a statement of its desired result."). The inventors' disclosed experiment was an experiment on the dermal cells.

Prosecution History

As explained in detail in Plaintiffs' opening brief, and by the PTO, the prosecution history supports Plaintiffs' interpretation because, when the Examiner misstated that the recited adenosine concentration should be applied "to the skin," the applicants "expressly corrected the Examiner." *See* Opening Br. at 15-16 (quoting '327 Reconsideration Denial at 9-10 (App'x A0221-22)). The applicants also submitted further experimental testing during prosecution, in which adenosine in the recited range was applied directly to dermal fibroblasts to demonstrate its effect, further confirming they intended the claimed range of adenosine to be applied "to the dermal cells." *See* Opening Br. at 16-17.

Defendant tries to convince this Court to use the asserted patents' prosecution history to rewrite the claims. But Defendant cannot meet, and does not even acknowledge, its "exacting" burden to show an "unambiguous disavowal[ ]" of the claim language's plain and ordinary meaning. *Thorner v. Sony Computer Entm't Am. LLC*, 669 F.3d 1362, 1366 (Fed. Cir. 2012); *Grober v. Mako Prods., Inc.*, 686 F.3d 1335, 1341 (Fed. Cir. 2012). Not only does no disavowal exist, the prosecution history supports Plaintiffs.

Save reprising its misconstruction of a "composition comprising a concentration of adenosine" as a "composition that is limited to a concentration of adenosine" in the draft claims of the asserted patents, Defendant repeats the same arguments already debunked in Plaintiffs' opening brief, as well as in four separate decisions by the PTO. As explained in those materials, in prosecution, the inventors distinguished the relevant prior art on the grounds it disclosed an increase in dermal cell proliferation, the "exact opposite" of the invention disclosed in the '327 Patent, and submitted further testing results to the Examiner in which they applied adenosine in the relevant range (10^{-4} M and 10^{-5} M) to dermal cells, causing no proliferation. '327 File History at 84 (App'x A0078); *see also* Opening Br. at 15-20. Defendant argues that the prior art under discussion during prosecution did not in fact disclose an increase in dermal cell proliferation, but that is irrelevant to whether the inventors distinguished it on that basis. As such, *Amgen Inc. v. Coherus Biosciences, Inc.*, in which the applicants "set forth multiple bases to distinguish between its invention and the cited prior art," is inapposite. 931 F.3d 1154, 1159-60 (Fed. Cir. 2019); *see also* '327 Reconsideration Denial at 8 (App'x A0220) (the inventors "did not use this statement to distinguish the claimed adenosine concentration from a concentration disclosed in the prior art").

Defendant also argues that where the inventors expressly corrected the Examiner when, in the '327 Patent Notice of Allowability, the Examiner misstated

the claims as reciting an adenosine concentration applied "to the skin," but did not reiterate that correction when a similar error appeared later in the '513 Patent Notice of Allowability, the inventors disclaimed the limitation "applied to the dermal cells." But the Federal Circuit has rejected the proposition that "a patentee's silence in the face of an examiner's unilateral statements in a Notice of Allowance amounts to a clear disavowal of claim scope." *Salazar v. Procter & Gamble Co.*, 414 F.3d 1342, 1346 (Fed. Cir. 2005); *see also Cree, Inc. v. SemiLEDs Corp.*, No. CIV.A. 10-866-RGA, 2012 WL 975697, at *17 (D. Del. Mar. 21, 2012) ("The examiner's remarks were thus unilateral in nature, and the unilateral remarks of an examiner cannot narrow a claim.") (citing *Salazar* 414 F.3d at 1347). *Biogen, Inc. v. Berlex Labs., Inc.* is not on point. 318 F. 3d 1132, 1138-39 (Fed. Cir. 2003) (noting the applicant's "response" to the Notice of Allowability, which was "consistent with the [applicant's] other prosecution statements" supporting disclaimer).

The '370 application makes no difference to Defendant's disclaimer argument. During prosecution of that application, and similarly to its statements in prosecution of the '372 Patent, the applicants distinguished certain prior art (the '649 patent) on the basis that it "increase[s] cell proliferation," including because it discloses using adenosine at a "far higher" level "than applicants' claimed range of concentrations." Ex. 4 (excerpts of the file history of the '370 application) ("'370 File History") at 6-7 (App'x A0152-53). Although the applicants noted that the '649

patent recites "percentages of ATP" by "weight of the composition," *id.*, at no point did the applicants state their own invention also recites percentages by weight of the composition, although this prosecution history makes clear they knew how to do so. *See* '327 IPR Denial at 11-12 n.5 (App'x A0182-83) ("[T]he arguments made by Patent Owner in connection with the '370 application are substantially similar to those it made – and disclosed to the Board – in connection with prosecution of the application discussed herein. As such, we consider the arguments based the '370 application to be cumulative to arguments already of record.").

3. The Court Should Strike Defendant's Expert Declaration

The Federal Circuit has opined that extrinsic evidence is "less reliable" than the intrinsic evidence. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1318 (Fed. Cir. 2005). "[E]xtrinsic evidence consisting of expert reports and testimony is generated at the time of and for the purpose of litigation and thus can suffer from bias that is not present in intrinsic evidence." *Id.* For that reason, this Court instructed the Parties that it will "review extrinsic evidence only if the Court is unable to construe the disputed claim terms based on the intrinsic evidence." D.I. 46 ¶ 16 (citing *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996) ("Only if there were still some genuine ambiguity in the claims, after consideration of all available intrinsic evidence, should the trial court have resorted to extrinsic evidence, such as expert testimony, in order to construe claim 1.")).

Although the intrinsic evidence unambiguously supports Plaintiffs' plain and ordinary meaning construction, Defendant nonetheless disclosed the testimony of Dr. Kasting with its opposition brief on February 5, 2020. But Defendant refused to allow its proffered expert to sit for deposition. *See* Ex. 16 (February 2020 email exchange between counsel) (App'x A0340-43). "The effect of" the "bias" of claim construction expert testimony "can be exacerbated" if "the expert's opinion is offered in a form that is not subject to cross-examination." *Phillips*, 415 F.3d at 1318. The Court should strike or disregard Dr. Kasting's testimony because it is unnecessary to construe the disputed term, such testimony is generally unreliable, and the effect of that unreliability is exacerbated by Defendant's refusal to allow Dr. Kasting to sit for a deposition.

Moreover, Dr. Kasting's testimony is clearly at odds with the claim construction mandated by the intrinsic evidence, purporting to interpret the patents on the basis of legal argument or proffered scientific facts that are largely irrelevant. Putting aside Dr. Kasting's parroting of arguments made by his client and already addressed above, he argues that because the patent does not "contain any description of how to determine the adenosine concentration at the dermal layer," it must therefore not mean the adenosine concentration is "applied to the dermal cells," as the claims plainly state. Kasting Dec. ¶ 30 (App'x A0258-59). This argument is most notable for what it omits, because Dr. Kasting does not opine that a POSITA would

not know how to determine the amount of adenosine, or any other ingredient, that penetrates to the dermal layer.

Dr. Kasting also says that when "topical skin products" are "marketed to the public" it is "common to describe" the "ingredients of the composition" by "weight percentages" for example, listing "2.5%" of "lidocaine" in the ingredient list for "EMLA Cream." Kasting Dec. ¶ 16 (App'x A0247-50). Dr. Kasting muses that it would be "strange" for "a skin care product to be described with reference to the concentration of [its] component that reaches a certain part of the skin," *id.*, and therefore concludes that the claims of the asserted patent must refer to the weight percentage of adenosine in the composition itself, as opposed to the amount that is "applied to the dermal cells," as the claim language specifies. This argument is flimsy at best. The asserted patents do not teach a "skin care product" that is "marketed to the public," but a method for enhancing the condition of skin in which a step of the disclosed method is that adenosine in the claimed range is "applied to the dermal cells." Nor do the claims describe "ingredients" in "weight percentages" like "2.5%," but instead disclose the molar concentration (e.g., "10^{-4} M to 10^{-7} M") of the adenosine that is "applied to the dermal cells."

It is inappropriate to use expert testimony to "erase limitations or otherwise diverge from the description of the invention as contained in the patent documents." *Aqua-Aerobic Sys., Inc. v. Aerators Inc.*, 211 F.3d 1241, 1245 (Fed. Cir. 2000).

Dr. Kasting's declaration is unreliable and contains omissions, and Defendant refused to allow him to sit for deposition or be cross-examined on his testimony. Dr. Kasting's testimony should be stricken or ignored.

4. Conclusion

Plaintiffs respectfully request the Court order the disputed term should have its plain and ordinary meaning, as well as order that Defendant may not continue press its convoluted and incorrect construction in, for example, expert reports or to the jury. To the extent the Court adopts a construction to clarify what the plain and ordinary meaning of the claims are, Plaintiffs respectfully request the Court adopt their alternative construction, which confirms the ordinary meaning of the term, that the adenosine concentration applies to the dermal cells in the claimed ranges.

IV. DEFENDANT'S SUR-REPLY POSITION

A. Introduction

Plaintiffs assert that "applied to the dermal cells" means "reaches the dermal cell layer." But Plaintiffs cite ***nothing*** in the intrinsic record making such a statement.

By contrast, L'Oréal USA's "applied to the skin containing the dermal cells" ordinary-meaning construction comes directly from the Summary of the Invention of the patents-in-suit. (*Supra* at 32-34.) And Applicants expressly relied upon the Summary of the Invention when introducing the asserted claims in their final form

during prosecution, explaining that they "all are based on the application of certain concentrations of adenosine ***to the skin*** to achieve certain results." (*Supra* at 38-40.) Applicants then proceeded to repeatedly distinguish multiple prior art references, including Hartzshtark, on the basis of the adenosine concentration applied ***to the skin***. (*Supra* at 40-43, 46-47, 49-50.) After reviewing all of these statements, the Examiner made explicit—twice—that the ordinary meaning of the disputed claim term refers to administering "adenosine at a concentration of 10^{-4} M to 10^{-7} M [or "10^{-3} M to 10^{-7} M"], ***to the skin.***" (*Supra* at 43, 47.)[33]

Plaintiffs' reply either ignores or attempts to sidestep these objective facts as well as other intrinsic evidence. Instead, Plaintiffs repeatedly refer to the Board's erroneous claim construction analysis that focused primarily on the "dermal cell" claim language. But as explained in L'Oréal USA's answering brief and below, this analysis and Plaintiffs' reply arguments are contrary to the intrinsic record as well as established claim construction principles, and should be rejected.

[33] Plaintiffs also do not, because they cannot, dispute that "dermal" application as used in the relevant art means application to the skin. (Kasting Decl., ¶ 14 (citing contemporaneous scientific literature) (Appx A0246-47).)

B. The Board's Claim Construction Ruling Is Incorrect and Should Not Be Followed

Plaintiffs continue to focus less on the intrinsic evidence and more on the Board's claim construction conclusions.[34] The Board, however, overlooked and misapprehended crucial intrinsic evidence and controlling Federal Circuit precedent (*e.g.*, *supra* 24-26), and was unaware that Plaintiffs' infringement contentions "now contend that L'Oréal USA's products containing the ***identical concentrations of adenosine that Applicants distinguished during prosecution*** (*e.g.*, 0.1% adenosine) somehow infringe the patents-in-suit" (*supra* at 21).[35]

Contrary to Plaintiffs' assertion, the latter point does not involve construing the asserted claims with reference to the accused products, rendering their cited cases (*supra* at 54) inapposite. Rather, this information provides permissible and "meaningful context for . . . claim construction," *Wilson Sporting Goods Co. v. Hillerich & Bradsby*, 442 F.3d 1322, 1326-27 (Fed. Cir. 2006),[36] which the mere

[34] Plaintiffs refer to "four separate decisions" (*supra* at 53, 63), but they were largely identical with respect to the two patents at issue.

[35] The above-quoted language from L'Oréal USA's answering brief refutes Plaintiffs' assertion that it is not "even clear what Defendant believes the import is of Plaintiffs' infringement contentions" (*supra* at 53-54).

[36] Plaintiffs' reliance on an unpublished Northern District of California decision regarding what *Wilson* "compel[s]" a court to consider does not, and cannot, override *Wilson* and its progeny's clear guidance. *See, e.g.*, *In re ICON Health & Fitness, Inc.*, 496 F.3d 1374, 1379 (Fed. Cir. 2007) (citing *Wilson* for the proposition that "an infringement or invalidity analysis provides the context for claim construction"); *Serio-US Indus., Inc. v. Plastic Recovery Techs. Corp.*, 459 F.3d 1311, 1319 (Fed.

existence of the instant litigation did not reveal (notwithstanding Plaintiffs' claim to the contrary). In any event, Plaintiffs' attempted distraction cannot change that the Board did not know that Plaintiffs' proposed claim construction is designed to capture the very same adenosine concentrations they distinguished to obtain their patents before the PTO.[37]

C. The Intrinsic Evidence Supports L'Oréal USA's Construction

1. The Claim Language

Plaintiffs do not dispute that the patents-in-suit employ well-established principles of claim drafting under which a new claim element (here, the adenosine concentration) is introduced by the indefinite article "a" and further defined by the definite article "the" (as well as the use of "wherein"). (*Supra* at 27-29.)[38] Instead, Plaintiffs contend that the use of the transitional phrase "comprising" somehow alters the meaning of this standard claim structure to allow "more adenosine" to be counted among the "other ingredients" that can be present.[39] (*Supra* at 57.)

Cir. 2006) ("[A] trial court may consult the accused device for context that informs the claim construction process.").

[37] The Court should not countenance Plaintiffs' attempt to blur its positions before the *PTO* in obtaining these patents and in defending them before the *Board*. (*See, e.g.*, *supra* at 55, 63.)

[38] Plaintiffs incorrectly assert that "the claim language twice refers to ***a*** 'concentration' of adenosine" (*supra* at 57); consistent with the case law ignored by Plaintiffs, the phrase "a concentration" appears only once.

[39] Plaintiffs' generic discussion of the structure of skin (*supra* at 52, 56-58) attempts to evade the proper claim construction analysis. *Phillips v. AWH Corp.*, 415 F.3d

As the Federal Circuit has explained, however, "'comprising' is not a weasel word with which to abrogate claim limitations." *Dippin' Dots, Inc. v. Mosey*, 476 F.3d 1337, 1343 (Fed. Cir. 2007). As a result, the term does not render each limitation in the claim open-ended, as Plaintiffs argue. *See, e.g.*, *Dippin' Dots*, 476 F.3d at 1343 ("The presumption raised by the term 'comprising' does not reach into each of the six steps to render every word and phrase therein open-ended—especially where, as here, the patentee has narrowly defined the claim term it now seeks to have broadened."); *Raytheon Co. v. Sony Corp.*, 727 F. App'x 662, 672 (Fed. Cir. 2018) (non-precedential) (same); *Bd. of Regents of the Univ. of Tex. Sys. v. BENQ Am. Corp.*, 533 F.3d 1362, 1372-73 (Fed. Cir. 2008) (same).[40]

In an attempt to reconcile the problems associated with their proposed construction (*supra* at 29-30), Plaintiffs assert that the adenosine concentration referred to in the dependent claims can only be what they characterize as the "numerical range" concentration (*supra* at 59). But the dependent claims do not mention "dermal cells" at all, and instead refer to a single concentration ("the adenosine concentration"). The natural conclusion is that, consistent with the claims themselves and the specification disclosure, claim 1 involves only "a" single

---

1303, 1321 (Fed. Cir. 2005) (en banc) ("[T]he 'ordinary meaning' of a claim term is its meaning to the ordinary artisan after reading the entire patent.").

[40] What "comprising" does allow is additional, ***unclaimed*** elements, *e.g.*, *Dippin' Dots*, 476 F.3d at 1343, but that is irrelevant to the meaning of the disputed language.

"concentration of adenosine," namely the concentration topically applied to the skin.[41]

2. The Specification

Like the Board, Plaintiffs attempt to support their proposed construction with a reference in the specification to "penetration" following the words "topical application" and disclosure of *ex vivo* experiments[42] using specific adenosine concentrations falling "***within*** the claimed ranges." (*Supra* at 60.) But Plaintiffs are unable to identify any portion of the specification that describes topically applied adenosine that "reaches the dermal cell layer" at the claimed concentration ranges. More importantly, Plaintiffs have no answer for the fact that ***the only portions of the specification discussing the concentration ranges appearing in the claims*** expressly refer, in the "Summary of the Invention," to the concentration "***applied to the skin***." (*Supra* at 33.)

[41] This link between the topical adenosine concentrations applied to the skin and the dependent claims is confirmed by the '327 patent prosecution. (*Supra* at 38-40.) Moreover, that dependent claim 9 recites a "transdermal delivery agent" (*supra* at 59) is irrelevant because the degree of adenosine skin penetration—which is not at all addressed in the specification—says nothing about how claim 1 defines the claimed adenosine concentration levels.

[42] Plaintiffs ignore that the Summary of the Invention states that these *ex vivo* experiments form the "bas[is]" for the claimed concentration ranges being "applied to the skin" (*supra* at 32-35 (citing '327 patent, 1:36-2:16, 2:38-40)), and misstate L'Oréal USA's position by suggesting that it contends these experiments are relevant to only one embodiment (*supra* at 61).

Plaintiffs assert that the specification's disclosure relating to increasing "DNA synthesis," "protein synthesis," and "cell size" are "not . . . embodiment[s] of the patented method, but a description of its results." (*Supra* at 61.) This once again ignores the Summary of the Invention, wherein each of these embodiments are described in terms of the claimed adenosine concentration ranges (*i.e.*, the "therapeutically effective amount") being "applied to the skin." (*Supra* at 32-33.)

3. The Prosecution History

Plaintiffs' prosecution history discussion in reply simply rehashes the flawed arguments from their opening and fails to respond to the evidence adduced in L'Oréal USA's answering brief.

First, Plaintiffs yet again ask the Court to view the prosecution history solely through the lens of disclaimer, as the Board did, even though the Federal Circuit has made clear that the prosecution history evidences both the "ordinary meaning of the term" and "how the PTO and the inventor understood the patent." (*Supra* at 36-37 & n.23.) Plaintiffs have not responded to this case law at all.[43] And it is directly applicable here in view of, for example, Plaintiffs characterizing the asserted claims as covering "the ***application*** of certain concentrations of adenosine ***to the skin*** to

[43] Instead, Plaintiffs contend that L'Oréal USA did not acknowledge the standard for prosecution disclaimer, which is incorrect and in any event unnecessary to apply here. (*Supra* at 37 n.23, 52 n.31.)

achieve certain results." (*Supra* at 40.) Plaintiffs noticeably ignore this statement, which tracks the Summary of the Invention passages discussed above.

Second, Plaintiffs repeat their incorrect assertion that they "expressly corrected" the Examiner's statement in the Reasons for Allowance and, in doing so, highlight the Board's erroneous reliance on this alleged correction. (*Supra* at 62.) That characterization simply does not accurately reflect the record, (*supra* at 43-45), and is further undermined by the fact that the Examiner ***repeated the very same conclusion*** during the '513 patent prosecution, where Applicants and the Examiner again focused on the concentrations to be applied to the skin. (*Supra* at 46-48.)

The reason for this is clear: Even setting aside the ordinary meaning of the disputed claim term made clear by the intrinsic evidence discussed above, Applicants consistently characterized the claims throughout prosecution as involving topically applying the recited adenosine concentrations "to the skin," and the Examiner understood them as such. (*Supra* at 38-48.)[44] The Examiner's statement was thus not a one-off "unilateral" remark (*supra* at 63-64), but rather one of many statements spanning five years of prosecution reflecting a common understanding of the claimed subject matter.[45] Moreover, contrary to Plaintiffs'

[44] Tellingly, Plaintiffs (like the Board) address neither the history of the pertinent claim language (*supra* at 38-40) nor Applicants' explanation of the meaning of that language (*supra* at 39-40).

[45] It bears noting that Plaintiffs are trying to have it both ways: They argue that, on the one hand, the alleged "correction" is essential to understanding the '327

assertion (*id.*), they were not silent in the face of the Examiner's Reasons for Allowance, but expressly agreed with them, providing additional evidence of the term's meaning. (*Supra* at 47-48; '513 prosecution history at 83 (Appx A0145).) For at least that reason, Plaintiffs' disclaimer cases (*supra* at 63-64) are inapposite.

Third, Plaintiffs continue to incorrectly assert that the "relevant prior art" was distinguished on the basis of cell proliferation. (*Supra* at 63.) Yet none of Plaintiffs' briefing identifies where exactly they allegedly distinguished Hartzshtark on the basis of cell proliferation, as opposed to the adenosine concentration applied to the skin. (*Supra* at 40-41, 43, n.28.) Plaintiffs likewise ignore the von Borstel patent. (*Supra* at 47.) And while the Applicants sought to distinguish DE107 ***in part*** on the basis of cell proliferation, that does not change that they also distinguished that reference based on the adenosine concentration applied to the skin. (*Supra* at 41-42.) For that reason, *Amgen* is applicable, and each of Applicants' "separate arguments," including their direct comparison of the adenosine composition concentrations, is relevant to claim scope. 931 F.3d at 1159-60.[46]

Fourth, and for much the same reason, Plaintiffs' attempt to dismiss the significance of the '370 application prosecution also fails. Contrary to Plaintiffs'

---

prosecution history, while the absence of a correction in the '513 patent prosecution history is irrelevant. Neither assertion passes muster, especially in view of the intrinsic record as a whole.

[46] Nor does Applicants' disclosure of additional *ex vivo* experimental data involving fibroblasts cultured in 10^{-4} M adenosine change the scope of the claims. There is no

assertions (*supra* at 64-65 (purporting to quote prosecution history)), Applicants stated—separate and apart from any "proliferation" issue—that it was "more important[]" to compare the concentrations in the prior art "composition[s]" to those in the claims, thereby further confirming that they correspond to the concentration applied to the skin. (*Supra* at 49-50 (actually quoting '370 application prosecution history).) Notably, in responding to these many prior art rejections in multiple prosecutions, Applicants ***never*** stated their claims were directed to the adenosine concentration that "reaches the dermal cell layer," as opposed to the concentration applied to the skin.

D. Dr. Kasting's Declaration Is Proper Claim Construction Evidence

L'Oréal USA respectfully requests that the Court deny Plaintiffs' request to strike the declaration of Professor Gerald Kasting, Ph.D.[47] The Federal Circuit has recognized that "expert testimony can be useful to a court . . . to provide background on the technology at issue, to explain how an invention works, to ensure that the court's understanding of the technical aspects of the patent is consistent with that of

---

reason to treat this data any different than the experimental data disclosed in the patents-in-suit, which is explained to be the "bas[is]" for 10^{-3} M to 10^{-7} M adenosine being the "therapeutically effective amount" to be "applied to the skin." (*Supra* at 32-35.)

[47] In making this request, which is in effect a motion to strike, Plaintiffs neither sought to meet and confer with L'Oréal USA nor provided the certification required by D. Del. LR 7.1.1. This alone is reason enough to deny their request.

a person of skill in the art, or to establish that a particular term in the patent or the prior art has a particular meaning in the pertinent field." *Phillips*, 415 F.3d at 1318. Dr. Kasting's declaration fits squarely within these parameters. Plaintiffs acknowledge as much by not challenging Dr. Kasting's expertise and by actually relying on the scientific principles discussed in his declaration (*see supra* at 56-57, 59, 60), thus belying their unsupported assertion that his testimony is somehow "unreliable" (*supra* at 66-68).

In addition to crediting the technological background provided by Dr. Kasting, Plaintiffs do not dispute that: (1) "dermal administration" is used to describe the application of products "directly to the surface of the skin" (Kasting Decl., ¶ 14 (Appx A0246-47)); and (2) topical skin products are typically described with reference to the active ingredient concentration in the composition (*id*, ¶ 16 (Appx A0247-50)). Plaintiffs attempt to minimize the latter fact by asserting that the patents-in-suit "do not teach a 'skin care product'" (*supra* at 67), but this is contradicted by their infringement allegations against certain of L'Oréal USA's skin care products (*supra* at 22; D.I. 13 at ¶ 31). Equally unavailing is Plaintiffs' assertion that the claims do not "describe 'ingredients' in 'weight percentages,'" but instead disclose their "molar concentration[s]." (*Supra* at 67.) As explained by Dr. Kasting, these are simply two ways of representing the concentration of an ingredient (Kasting Decl., ¶ 16 n.1 (Appx A0248)) and, in fact, Applicants confirmed this very

point during prosecution (*supra* at 41 (citing '327 prosecution history at 84 (Appx A0078)).[48]

Finally, contrary to Plaintiffs' assertions, L'Oréal USA did not refuse to produce Dr. Kasting for a deposition. Rather, L'Oréal USA explained that Dr. Kasting was unavailable during the narrow timeframe in which Plaintiffs sought the deposition due to significant prior academic commitments, and that claim construction depositions were not contemplated by the Scheduling Order. (*See* Feb. 7, 2020 Email (Appx A0341).) Because Dr. Kasting's Declaration is proper claim construction evidence and Plaintiffs have not shown that exclusion is warranted, their request should be denied.

E. Conclusion

L'Oréal USA respectfully submits that the Court should adopt its proposed construction for the reasons set forth above.

[48] Plaintiffs' attempt to contort Dr. Kasting's opinions notwithstanding (*supra* at 66-67), what matters for claim construction purposes is that there is no discussion in the specification of any specific concentration that reaches the dermal layer after topical administration (*see* Kasting Decl., ¶ 30 (Appx A0258-59)).

DATED: March 6, 2020

Respectfully submitted,

FARNAN LLP

/s/ Brian E. Farnan

Brian E. Farnan (Bar No. 4089)
Michael J. Farnan (Bar No. 5165)
919 North Market Street, 12th Floor
Wilmington, DE 19801
Telephone: (302) 777-0300
Facsimile: (302) 777-0301
bfarnan@farnanlaw.com
mfarnan@farnanlaw.com

Of Counsel:
William Christopher Carmody
Tamar E. Lusztig
Beatrice C. Franklin
SUSMAN GODFREY L.L.P.
1301 Avenue of the Americas, 32nd Floor
New York, NY 10019
Telephone: (212) 336-8330
Facsimile: (212) 336-8340
bcarmody@susmangodfrey.com
tlusztig@susmangodfrey.com
bfranklin@susmangodfrey.com
Justin A. Nelson
SUSMAN GODFREY L.L.P.
1000 Louisiana Street, Suite 5100
Houston, Texas 77002
Telephone: (713) 651-9366
Facsimile: (713) 654-6666
jnelson@susmangodfrey.com

Attorneys for University of Massachusetts and Carmel Laboratories, LLC

Matthew B. Lowrie
FOLEY & LARDNER LLP
111 Huntington Avenue, Suite 2600
Boston, MA 02199
Telephone: (617) 342-4000
Facsimile: (617) 342-4001
mlowrie@foley.com

Attorneys for Carmel Laboratories, LLC

COMMONWEALTH OF MASSACHUSETTS,

By its attorney,

MAURA HEALEY
ATTORNEY GENERAL

By: *William Christopher Carmody*
William Christopher Carmody
Special Assistant Attorney General
SUSMAN GODFREY L.L.P.
1301 Avenue of the Americas, 32nd Floor
New York, NY 10019
Telephone: (212) 336-8330
Facsimile: (212) 336-8340
bcarmody@susmangodfrey.com

Attorney for University of Massachusetts Medical School

/s/ Katharine L. Mowery
Frederick L. Cottrell, III (#2555)
Jeffrey L. Moyer (#3309)
Katharine L. Mowery (#5629)
RICHARDS, LAYTON & FINGER, P.A.

One Rodney Square
920 N. King Street
Wilmington, Delaware 19801
(302) 651-7700
cottrell@rlf.com
moyer@rlf.com
mowery@rlf.com
Attorneys for Defendant
L'Oréal USA, Inc.

OF COUNSEL:

Eric W. Dittmann
Isaac S. Ashkenazi
Nicholas A. Tymoczko
PAUL HASTINGS LLP
200 Park Avenue
New York, NY 10166

Dennis S. Ellis
Katherine F. Murray
Serli Polatoglu
PAUL HASTINGS LLP
515 South Flower Street, 25th Floor
Los Angeles, CA, 90071
(213) 683-6000

Naveen Modi
Joseph E. Palys
PAUL HASTINGS LLP
875 15th Street, N.W.
Washington, D.C., 20005
(202) 551-1990

PARTIES' WORD COUNT CERTIFICATION

The above-signed counsel hereby certify that Each Claim Construction Brief complies with the type volume requirements set forth in the Court's Scheduling Order (D.I. 21). Counsel certify that the Opening Claim Construction Brief contains less than 5,500 words, the answering brief contains less than 8,250 words, the reply brief contains less than 5,500 words, and the sur-reply brief contains less than 2,750 word, which were counted by each parties respective counsel using the word count feature in Microsoft Word, in 14-point Times New Roman font. The foregoing word counts do not include the cover page, tables of contents and authorities, tables, headings, or signature blocks.